

Supplementary Table 1:**Read numbers of perfectly mapped reads in all 3 biological replicates.**

	genotype	total reads E+06	miRNA reads E+06	% miRNA of total
replicate 1	wildtype	24	15	65
	<i>Adarb1</i> ^{-/-}	21	11	51
	<i>Adar</i> ^{-/-} , <i>Adarb1</i> ^{-/-}	23	10	46
replicate 2	wildtype	20	7	36
	<i>Adarb1</i> ^{-/-}	16	4	25
	<i>Adar</i> ^{-/-} , <i>Adarb1</i> ^{-/-}	15	3	20
replicate 3	wildtype	29	11	40
	<i>Adarb1</i> ^{-/-}	30	13	43
	<i>Adar</i> ^{-/-} , <i>Adarb1</i> ^{-/-}	28	13	46

Supplementary Table 2:

Consistently deregulated miRNAs in mice deficient in ADARs

miRNAs consistently deregulated (more than 1.3 fold) in *Adarb1*^{-/-} and *Adar*^{-/-}, *Adarb1*^{-/-} mice (sorted by fold change in *Adarb1*^{-/-}). The underlined miRNAs are known edited ones or have been identified as edited in this study. In bold are the fold changes that are consistent over all biological replicates (Students t-test: P<0.1).

consistently deregulated miRNAs	fold change in <i>Adarb1</i> ^{-/-}	P-value	fold change in <i>Adar</i> ^{-/-} , <i>Adarb1</i> ^{-/-}	P-value	possible editing context near DROSHA cleavage site	possible editing context near DICER1 cleavage site
let-7b	-2.50	0.000	-1.10	0.446	-	UAA
let-7c	-2.02	0.000	-1.59	0.106	-	UAG, UAA
miR-184	-1.89	0.010	-1.51	0.002	UAG	-
let-7d	-1.80	0.003	-1.61	0.056	UAG	UAG
let-7i	-1.79	0.018	-1.74	0.090	UAG	UAA
miR-124	-1.72	0.000	-1.59	0.007	-	UAA
miR-204	-1.70	0.015	-1.44	0.000	-	-
miR-551b	-1.69	0.003	-1.25	0.210	-	-
miR-720	-1.60	0.001	-1.16	0.104	-	-
let-7f	-1.51	0.028	-1.51	0.038	-	UAA
<u>let-7g</u> ^[1]	-1.50	0.010	-1.39	0.105	-	UAA
miR-140*	-1.47	0.025	-1.31	0.180	-	UAG, UAC
let-7e	-1.44	0.001	-1.27	0.127		
let-7a	-1.43	0.011	-1.34	0.089		
miR-338-3p	-1.36	0.005	1.14	0.388		
miR-135a-2*	-1.30	0.008	-1.41	0.000		
miR-344	-1.26	0.130	-1.35	0.067		
<u>miR-3099</u> ^[6]	-1.15	0.190	-1.31	0.030		
<u>miR-376c</u> ^[1]	-1.14	0.362	-1.35	0.070		
miR-30b	-1.12	0.042	1.91	0.054		
miR-598	-1.09	0.371	-1.32	0.028		
miR-1839-5p	-1.08	0.311	-1.36	0.012		
miR-350*	-1.06	0.373	1.37	0.087		
miR-340-3p	-1.01	0.486	1.34	0.008		
miR-137	1.06	0.393	-1.53	0.011		
<u>miR-503</u> ^{*[1]}	1.13	0.309	1.30	0.028		
miR-540-5p	1.13	0.304	1.49	0.074		
miR-296-3p	1.15	0.325	1.40	0.045		
miR-325	1.16	0.364	1.37	0.096		
miR-362-5p	1.16	0.327	1.40	0.016		
miR-673-5p	1.17	0.442	-2.44	0.093		
miR-708*	1.17	0.141	1.52	0.064		
miR-126-5p	1.19	0.317	1.51	0.089		
miR-30e	1.19	0.269	1.44	0.044		
miR-29b	1.20	0.106	1.47	0.020		
miR-370	1.21	0.158	1.38	0.042		
miR-3062	1.21	0.106	1.42	0.004		
miR-30c	1.25	0.229	1.78	0.047		
miR-101a	1.26	0.153	1.39	0.029		
miR-329*	1.27	0.163	1.49	0.007		
miR-34c	1.27	0.031	1.38	0.021		

miR-1195	1.27	0.148	1.35	0.075		
miR-30a	1.28	0.179	1.35	0.021		
miR-486*	1.32	0.055	1.13	0.337		
<u>miR-17</u> * ^[4]	1.32	0.064	1.29	0.193		
miR-186*	1.32	0.287	1.48	0.001		
miR-410	1.33	0.012	-1.00	0.495		
miR-200a	1.34	0.010	1.47	0.008		
<u>miR-133a</u> * ^[1]	1.34	0.087	1.52	0.062		
miR-132	1.34	0.000	1.04	0.350		
miR-124*	1.35	0.091	1.18	0.140		
miR-466d-3p	1.35	0.008	1.24	0.301		
miR-139-5p	1.35	0.044	1.15	0.108		
miR-221	1.36	0.011	1.39	0.024		
miR-669l	1.36	0.075	1.32	0.207		
miR-384-5p	1.36	0.030	1.08	0.032		
miR-300*	1.37	0.024	1.10	0.199		
<u>miR-411</u> * ^[1]	1.38	0.004	1.12	0.305		
miR-34a	1.38	0.055	-1.07	0.125		
miR-196a	1.40	0.080	1.32	0.049		
miR-28	1.41	0.061	1.22	0.215		
miR-25	1.41	0.084	-1.03	0.455		
miR-32	1.42	0.265	1.67	0.054		
miR-210	1.42	0.199	-1.26	0.005		
miR-375	1.42	0.006	1.27	0.139		
miR-23a	1.42	0.039	1.16	0.047		
miR-200b*	1.43	0.046	1.18	0.279		
<u>miR-381</u> ^[6]	1.44	0.073	1.24	0.052		
miR-299	1.45	0.093	1.16	0.270		
miR-7a-1*	1.46	0.021	1.16	0.104		
miR-668	1.46	0.154	2.18	0.068		
miR-134	1.46	0.140	1.36	0.021		
miR-466i-3p	1.47	0.090	2.81	0.154		
<u>miR-142-5p</u> ^[3]	1.48	0.044	1.11	0.290		
miR-667*	1.48	0.016	1.31	0.040		
miR-669f-3p	1.48	0.025	1.51	0.232		
miR-380-3p	1.49	0.039	1.02	0.469		
miR-106b*	1.49	0.009	1.51	0.060		
miR-219-5p	1.50	0.066	1.29	0.240		
miR-19a	1.51	0.202	1.81	0.001		
miR-669a-5p	1.51	0.016	1.36	0.154		
miR-30c-1*	1.52	0.013	1.50	0.046		
miR-361	1.52	0.062	1.24	0.129		
miR-146b	1.52	0.054	1.25	0.079		
miR-200c	1.53	0.033	1.46	0.081		
miR-466p-3p	1.53	0.055	1.44	0.242		
miR-466e-3p	1.53	0.055	1.44	0.242		
miR-3095-3p	1.53	0.096	1.09	0.350		
miR-466b-3p	1.54	0.055	1.45	0.240		
miR-669o-5p	1.54	0.006	1.18	0.271		
<u>miR-379</u> * ^[6]	1.55	0.052	1.27	0.186		
<u>miR-144</u> * ^[5]	1.55	0.001	1.47	0.076		
<u>miR-532-5p</u> ^[1]	1.55	0.052	1.06	0.378		
miR-30c-2*	1.56	0.015	1.27	0.185		
miR-669c	1.56	0.024	1.50	0.019		
<u>miR-19b</u> ^[4]	1.58	0.167	1.81	0.000		
miR-466a-3p	1.61	0.038	1.43	0.250		

miR-18b	1.61	0.093	1.70	0.100		
miR-297b-3p	1.63	0.004	1.55	0.193		
miR-92a	1.64	0.000	1.24	0.255		
miR-369-3p	1.64	0.038	1.37	0.174		
miR-20a	1.66	0.076	1.32	0.121		
miR-20b*	1.66	0.014	1.81	0.059		
miR-1	1.67	0.011	1.17	0.287		
miR-3470a	1.68	0.018	1.48	0.074		
miR-1186b	1.70	0.014	1.22	0.068		
miR-363-3p	1.71	0.034	1.36	0.236		
miR-155	1.71	0.047	1.68	0.010		
miR-301a	1.72	0.137	1.72	0.015		
miR-467a	1.72	0.047	1.74	0.056		
miR-34b-5p	1.73	0.059	1.73	0.020		
miR-3473	1.75	0.020	1.72	0.121		
miR-297a	1.76	0.097	1.32	0.035		
<u>miR-376b</u> ^[1]	1.79	0.010	1.29	0.198		
miR-466n-3p	1.80	0.002	1.33	0.145		
<u>miR-450b-3p</u> ^[4]	1.81	0.031	1.25	0.111	-	UAC
miR-302c	1.82	0.071	1.94	0.174	-	-
miR-301b	1.84	0.054	1.52	0.098	-	UAC
miR-542-3p	1.85	0.072	1.55	0.001	-	UAC
miR-190	1.85	0.156	2.20	0.041	UAC	-
<u>miR-106a</u> ^[1]	1.86	0.062	1.55	0.223	UAG	-
miR-367	1.88	0.019	2.29	0.123	-	-
miR-335-3p	1.90	0.081	1.90	0.095	-	-
miR-19b-1*	1.96	0.055	1.52	0.055	UAG	UAC, UAG
miR-3106	1.98	0.078	2.36	0.140	-	UAC
miR-466c-5p	2.02	0.043	1.62	0.017	UAA	UAC
miR-493*	2.06	0.015	1.50	0.057	-	-
<u>miR-450b-5p</u> ^[4]	2.08	0.025	1.51	0.000	-	UAC
miR-574-5p	2.09	0.023	1.84	0.064	-	-
miR-20b	2.17	0.048	1.81	0.168	UAG	UAC
<u>miR-219-3p</u> ^{*[6]}	2.41	0.099	1.53	0.067	-	-
miR-712*	2.72	0.135	3.42	0.091	-	-
miR-690	3.35	0.123	1.69	0.063	-	UAA
miR-466i-5p	5.37	0.101	2.58	0.034	UAC	UAC

^[1] (Kawahara Y et al. 2008)

^[2] (Luciano DJ et al. 2004)

^[3] (Yang W et al. 2006)

^[4] (Landgraf P et al. 2007)

^[5] (Blow MJ et al. 2006)

^[6] (Chiang HR et al. 2010)

Supplementary Table 3:

Example for output of significance testing of A to G transitions in mature miRNAs.

The output for the significance of editing test for mmu-miR-378 transitions as mean of all replicates is shown per position of the reference sequence. The editing position (position 16 of mature miRNA) is marked in bold; underlined are the number of reads that have a G instead of an A at position 16.

wildtype					Adarb1 ^{-/-}					Adarb ^{-/-} , Adarb1 ^{-/-}					
Ref	A	C	G	T	Ref	A	C	G	T	Ref	A	C	G	T	
A	5356				A	5510				A	5496				
C	8	0	0	0	C	1	0	0	0	C	1	0	0	0	
T	58	57089	22	39	T	20	59094	15	38	C	16	58457	8	29	
G	22	47	11	57252	T	24	56	24	2	T	6	32	3	58530	
A	24	31	57268	26	G	30	33	1	22	G	16	18	7	15	
C	14	20	57313	23	G	16	25	3	27	G	7	16	9	20	
T	5726				A	5919				A	5850				
G	4	49	59	12	A	8	36	21	12	C	0	37	44	6	
A	31	57315	24	32	C	10	59215	8	43	C	7	58572	5	24	
C	19	32	8	57384	T	2	25	3	2	T	5	18	3	58600	
T	0	0	0	57455	T	0	0	0	5	T	0	0	0	58634	
G	0	0	57455	0	G	0	0	5928	5	G	0	0	5863	4	0
A	0	0	57455	0	G	0	0	5928	5	G	0	0	5863	4	0
C	5745				A	5928				A	5863				
T	5	0	0	0	A	5	0	0	0	A	4	0	0	0	
G	17	19	57377	41	G	13	20	0	52	G	21	22	3	37	
A	32	108	68	57203	T	35	111	88	7	T	42	134	112	58291	
C	12	57359	10	30	C	10	59176	11	38	C	5	58544	2	24	
T	5723				A	5912				A	5850				
G	6	37	125	8	G	1	32	49	21	A	2	19	39	8	
A	52	26	57300	21	G	66	24	6	29	G	57	23	1	62	
C	5732				A	5909				A	5848				
T	5	42	16	3	A	0	52	43	15	A	9	32	14	5	
G	5727				A	5910				A	5844				
A	7	64	12	5	G	4	53	18	13	G	9	21	10	12	
C	25	23	57253	22	G	43	28	1	31	G	18	19	3	20	
T	0	0	56574	0	G	0	0	5843	0	G	0	0	5756	1	0

Supplementary Table 4:

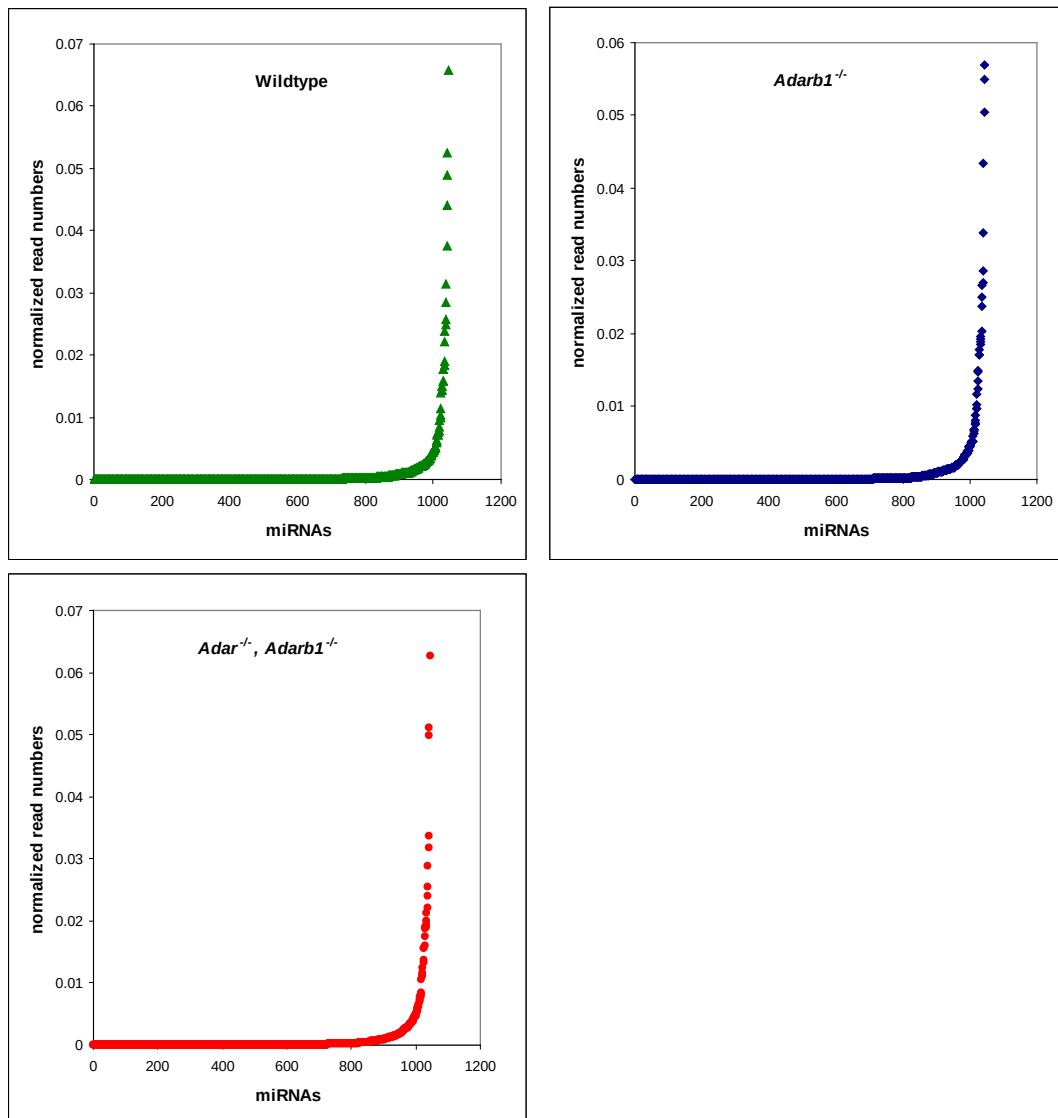
Significant editing events detected in at least 2 out of 3 replicates.

miRNAs in green have already been identified as edited mature miRNAs. The red A in the “context” column marks the edited adenosine, the nucleotide after the slash is the editing site opposing base. Plausible contexts according to editing site preferences are marked in bold, rather unusual target sites are in gray. The “position” column lists the nucleotide position of the edited adenosine in the mature miRNA. Positions in blue are located within the seed sequence of the miRNA.

miRNA	average read number	abundance in <i>Adarb1</i> ^{-/-} in % of wildtype	abundance in <i>Adar</i> ^{-/-} , <i>Adarb1</i> ^{-/-} in % of wildtype	editing in # biological replicates	position	context
miR-378	58589	101	88	2	16	CAG / U
miR-376b	13612	178	113	2	6	UAG / U
miR-1957	2704	127	181	2	15	UAU / U
miR-381	2206	145	118	3	4	UAC / U
miR-467d*	1145	146	201	2	9	UAC / C
miR-3099	684	87	77	2	7	UAG / C
miR-706	228	218	253	2	20	AAA / U
miR-1186	199	181	147	2	16	AAG / C
miR-3102-5p.2	196	106	95	2	18	GAG / U
miR-703	156	223	132	2	4	AAA / U
miR-669b*	89	192	130	2	4	UAU / C
miR-1966	80	140	124	2	20	GAG / U
miR-669h-3p	65	152	187	3	2	UAU / U
miR-669p*	56	275	373	2	23	UAU / U
miR-669p*	56	275	373	2	5	AAC / U
miR-669i	54	180	132	2	20	UAC / U
miR-1934*	52	305	262	2	7	GAC / U
miR-466h-3p	47	122	149	2	12	CAC / U
miR-293*	44	293	190	2	7	AAC / U
miR-344d	37	99	114	2	6	UAA / U
miR-1941-5p	36	182	217	2	15	UAC / U
miR-3092	33	164	159	2	2	GAA / C
miR-466f-5p	32	215	231	2	20	CAU / U
miR-504*	32	151	154	2	7	GAG / A
miR-3474	24	127	141	2	13	GAC / U
miR-1971	17	137	101	2	16	GAG / U
miR-1971	17	137	101	2	3	AAA / -
miR-1970	16	175	132	3	16	UAG / -
miR-146a*	15	301	142	2	8	AAA / U
miR-1298*	11	119	91	2	15	G <u>A</u> U / U

Supplementary Figure 1:

A small set of miRNAs contains the most abundant miRNAs in all genotypes and all biological replicates. Normalized read numbers of all detected miRNAs are plotted, showing that only few miRNAs are highly abundant.



References Supplement

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