Figure S1
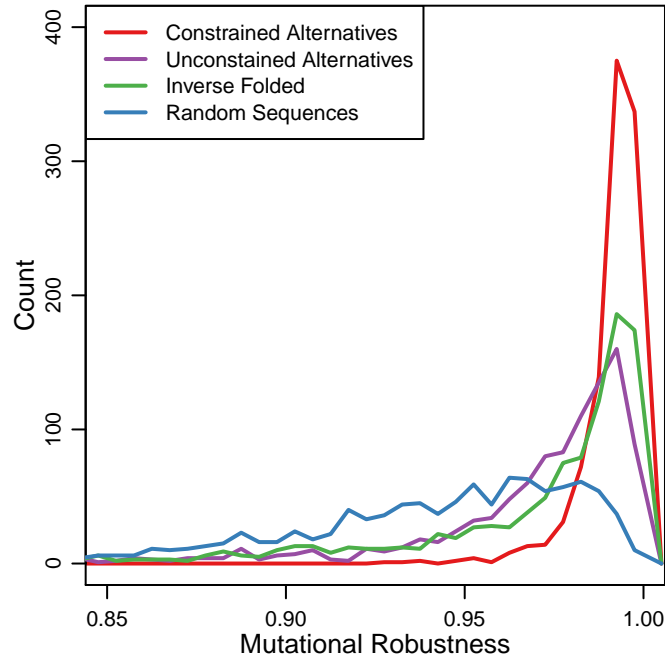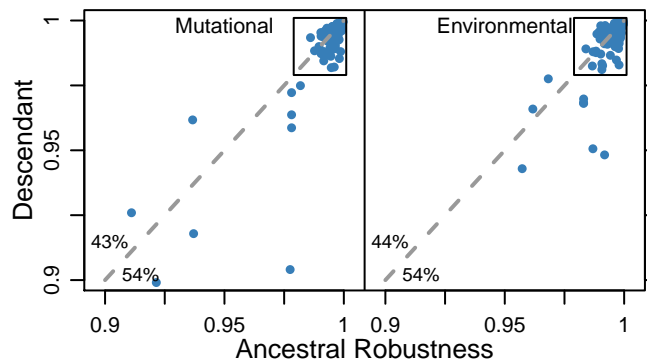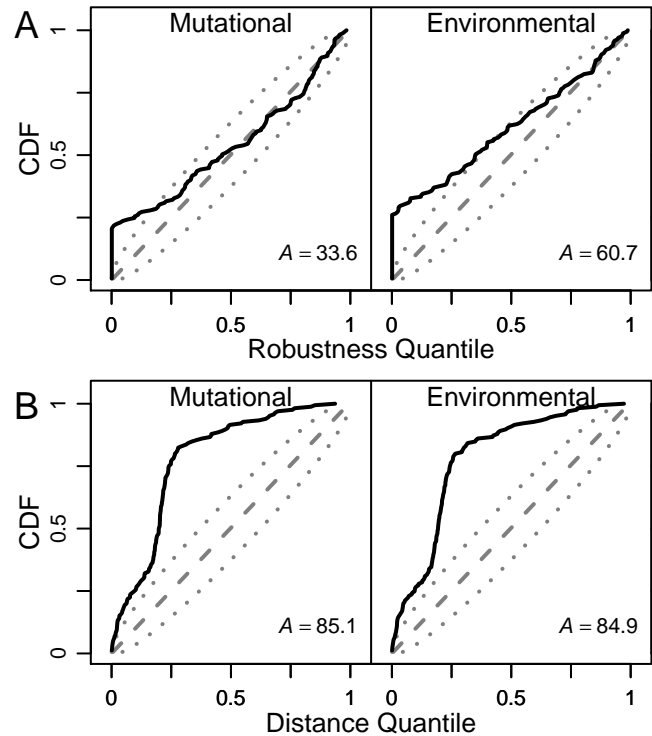

Four null distributions were generated for dps-mir-317. As described in Methods, constrained alternatives are simulated descendants of the inferred ancestor of dps-mir-317 that have the same structure as dps-mir-317. Unconstrained alternatives are simulated descendants with any structure. Inverse folded are random sequences that fold into the same structure following the method of Szöllosi and Derényi (2009). Random sequences have the same length as dps-mir-317 and residues drawn with equal frequencies.
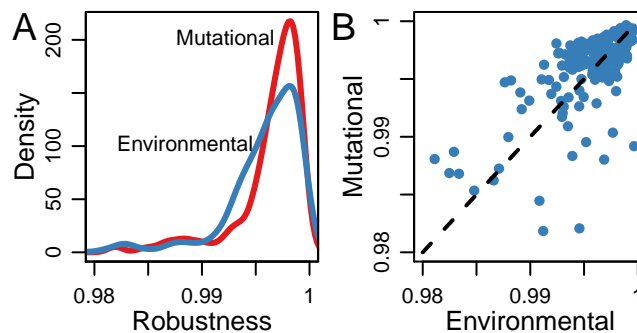
Figure S2

A version of Fig. 3 showing the outlying points and the regions shown in Fig. 3.

Figure S3

Test of the "inverted" selection hypothesis (see Results). We constructed a new null distribution of descendant pre-miRNA sequences. We took the structure-unconstrained set (Fig. 5) and removed the sequences with robustness lower than the median robustness (left panels r_m; right panels r_e). These null distributions, containing ≈ 500 sequences each, simulate strong directional selection for robustness in the absence of selection for structure. We find that such selection for mutational robustness would cause an overall increase in robustness (A), which we did not observe in our real dataset (Fig. 3). Additionally, such selection would still be insufficient to account for the lack of change in structure shown in Fig. 5B (B).

Figure S4

Mutational and environmental are skewed and correlated. (A) Distributions of mutational and environmental robustness for 221 natural pre-miRNAs. (B) Pairwise comparisons of mutational and environmental robustness of these sequences. (Spearman's rank correlation, $\rho = 0.729$).

Table S1: Results of Constrained Simulations

As described in Methods, we downloaded micro-RNA sequences from *Drosophila* species and estimated their ancestral sequences. For branches that had at least 1 substitution and no indels, we measured the mutational and environmental robustness of its ancestor and descendant and calculated the quantile of each descendant robustness with respect to a null distribution created by "replaying the tape" of evolution from its ancestor.

    Sub: number of substitutions between ancestor and descendant; '–' means that the branch contained indels. **Samp**: Number of samples in constrained null distribution. **Uniq:** Number of unique values of this robustness. **Anc:** Ancestral robustness **Desc:** Descendant robustness **Quant:** Quantile of descendant robustness with respect to constrained null.

micro-RNA	Sub	Samp	Mutational Robustness				Environmental Robustness			
			Uniq	Anc	Desc	Quant	Uniq	Anc	Desc	Quant
bantam-dan	1	58	47	0.997724	0.997724	0.578	52	0.996682	0.996651	0.431
bantam-der	0									
bantam-dgr	1	2	2	0.997724	0.995131	0.250	2	0.996687	0.996698	1.000
bantam-dme	0									
bantam-dmo	–									
bantam-dpe	0									
bantam-dps	0									
bantam-dse	0									
bantam-dsi	0									
bantam-dvi	1	2	2	0.997724	0.997667	0.750	2	0.996681	0.99669	1.000
bantam-dwi	0									
bantam-dya	0									
let-7-dan	5	1000	859	0.99875	0.997156	0.319	843	0.99826	0.998804	0.878
let-7-der	0									
let-7-dme	0									
let-7-dmo	1	65	60	0.998725	0.999121	0.946	56	0.998793	0.998681	0.292
let-7-dps	–									
let-7-dse	0									
let-7-dsi	0									
let-7-dvi	1	2	2	0.998725	0.998249	0.250	2	0.998791	0.99839	0.500
let-7-dwi	–									
let-7-dya	0									
mir-iab-4-dan	0									
mir-iab-4-der	0									
mir-iab-4-dgr	0									
mir-iab-4-dme	0									
mir-iab-4-dmo	0									
mir-iab-4-dpe	0									
mir-iab-4-dps	0									
mir-iab-4-dse	0									
mir-iab-4-dsi	0									
mir-iab-4-dvi	0									
mir-iab-4-dwi	1	1	1	0.991587	0.984463	0.500	1	0.992965	0.990852	0.000
mir-iab-4-dya	0									
mir-1-dan	–									
mir-1-der	–									
mir-1-dgr	–									
mir-1-dme	–									
mir-1-dmo	2	12	12	0.998449	0.998074	0.375	12	0.996504	0.996255	0.583
mir-1-dpe	–									
mir-1-dps	0									
mir-1-dse	0									
mir-1-dsi	0									
mir-1-dvi	–									

micro-RNA	Sub	Samp	Mutational Robustness				Environmental Robustness			
			Uniq	Anc	Desc	Quant	Uniq	Anc	Desc	Quant
mir-1-dwi	–									
mir-1-dya	0									
mir-2a-1-dan	–									
mir-2a-1-der	2	72	63	0.998805	0.998921	0.465	67	0.996629	0.998443	0.708
mir-2a-1-dgr	0									
mir-2a-1-dme	0									
mir-2a-1-dmo	4	1000	615	0.998297	0.99845	0.360	756	0.997813	0.99728	0.196
mir-2a-1-dpe	0									
mir-2a-1-dps	0									
mir-2a-1-dse	0									
mir-2a-1-dsi	0									
mir-2a-1-dvi	–									
mir-2a-1-dwi	9	666	587	0.999014	0.998908	0.766	630	0.999029	0.998906	0.733
mir-2a-1-dya	0									
mir-2a-2-dan	0									
mir-2a-2-der	0									
mir-2a-2-dgr	0									
mir-2a-2-dme	0									
mir-2a-2-dmo	0									
mir-2a-2-dpe	0									
mir-2a-2-dps	0									
mir-2a-2-dse	0									
mir-2a-2-dsi	0									
mir-2a-2-dvi	0									
mir-2a-2-dwi	0									
mir-2a-2-dya	0									
mir-2c-dan	–									
mir-2c-der	0									
mir-2c-dgr	–									
mir-2c-dme	0									
mir-2c-dmo	–									
mir-2c-dpe	0									
mir-2c-dps	0									
mir-2c-dse	0									
mir-2c-dsi	0									
mir-2c-dvi	0									
mir-2c-dwi	–									
mir-2c-dya	0									
mir-3-dan	11	324	317	0.993829	0.99634	0.352	317	0.996373	0.998185	0.525
mir-3-der	1	58	48	0.999209	0.999195	0.543	48	0.999113	0.999113	0.569
mir-3-dme	0									
mir-3-dmo	7	844	828	0.998122	0.997725	0.998	827	0.99674	0.995662	0.882
mir-3-dpe	0									
mir-3-dps	0									
mir-3-dse	0									
mir-3-dsi	1	58	47	0.999209	0.999208	0.586	46	0.999111	0.999111	0.500
mir-3-dvi	5	1000	966	0.998122	0.985339	0.412	972	0.996741	0.984785	0.312
mir-3-dwi	–									
mir-3-dya	1	58	48	0.999209	0.999339	0.991	49	0.999113	0.999116	0.698
mir-4-dan	0									
mir-4-der	0									
mir-4-dme	2	126	122	0.995025	0.997542	0.194	112	0.991995	0.996676	0.206
mir-4-dmo	0									
mir-4-dpe	0									
mir-4-dps	0									

micro-RNA	Sub	Samp	Mutational Robustness				Environmental Robustness			
			Uniq	Anc	Desc	Quant	Uniq	Anc	Desc	Quant
mir-4-dse	0									
mir-4-dsi	0									
mir-4-dvi	0									
mir-4-dwi	0									
mir-4-dya	0									
mir-5-dan	–									
mir-5-der	0									
mir-5-dme	1	65	57	0.997389	0.997332	0.315	61	0.996036	0.995801	0.200
mir-5-dmo	1	16	16	0.996689	0.995676	0.031	16	0.995875	0.995801	0.062
mir-5-dpe	0									
mir-5-dps	0									
mir-5-dse	1	3	3	0.997069	0.996989	0.167	3	0.996653	0.998036	0.000
mir-5-dsi	–									
mir-5-dvi	–									
mir-5-dwi	–									
mir-5-dya	1	56	50	0.996989	0.996817	0.116	54	0.99694	0.996803	0.179
mir-6-1-dan	–									
mir-6-1-der	1	5	5	0.997701	0.997445	0.900	5	0.996267	0.996245	0.800
mir-6-1-dgr	5	1000	965	0.990466	0.987244	0.285	964	0.990193	0.98709	0.112
mir-6-1-dme	1	93	84	0.997463	0.997492	0.699	93	0.994463	0.993908	0.258
mir-6-1-dmo	–									
mir-6-1-dpe	–									
mir-6-1-dps	0									
mir-6-1-dse	0									
mir-6-1-dsi	2	1998	1392	0.997649	0.996563	0.257	1524	0.996262	0.995226	0.268
mir-6-1-dvi	2	24	24	0.990466	0.993952	0.229	23	0.990188	0.997982	0.250
mir-6-1-dwi	–									
mir-6-1-dya	5	1000	907	0.997701	0.997755	0.747	908	0.996275	0.996301	0.599
mir-6-2-dan	7	1000	914	0.997011	0.997763	0.591	929	0.9959	0.998937	0.933
mir-6-2-der	–									
mir-6-2-dgr	–									
mir-6-2-dme	2	9	9	0.994417	0.994827	0.167	9	0.997543	0.997314	0.333
mir-6-2-dmo	5	196	193	0.996459	0.992893	0.209	192	0.99534	0.996163	0.883
mir-6-2-dpe	–									
mir-6-2-dps	–									
mir-6-2-dse	0									
mir-6-2-dsi	0									
mir-6-2-dvi	–									
mir-6-2-dwi	–									
mir-6-2-dya	3	1000	194	0.994224	0.989537	0.340	798	0.997416	0.99519	0.177
mir-6-3-dan	–									
mir-6-3-der	1	4	4	0.997212	0.997247	0.875	4	0.996602	0.997172	0.750
mir-6-3-dgr	–									
mir-6-3-dme	1	2	2	0.997212	0.99605	0.250	2	0.996597	0.994491	0.500
mir-6-3-dmo	8	506	492	0.993334	0.994931	0.597	493	0.99393	0.99602	0.453
mir-6-3-dpe	–									
mir-6-3-dps	1	7	7	0.99291	0.997044	0.929	7	0.99229	0.995941	0.286
mir-6-3-dse	0									
mir-6-3-dsi	0									
mir-6-3-dvi	–									
mir-6-3-dwi	–									
mir-6-3-dya	2	137	121	0.997212	0.998215	0.931	129	0.996605	0.996362	0.409
mir-7-dan	–									
mir-7-der	1	53	53	0.994738	0.994875	0.689	53	0.988211	0.988211	0.396
mir-7-dgr	–									

micro-RNA	Sub	Samp	Mutational Robustness				Environmental Robustness			
			Uniq	Anc	Desc	Quant	Uniq	Anc	Desc	Quant
mir-7-dme	0									
mir-7-dmo	3	1000	443	0.989602	0.989976	0.515	792	0.986977	0.987963	0.474
mir-7-dpe	0									
mir-7-dps	0									
mir-7-dse	0									
mir-7-dsi	0									
mir-7-dvi	–									
mir-7-dwi	–									
mir-7-dya	1	53	53	0.994738	0.994713	0.425	52	0.988221	0.98763	0.113
mir-8-dan	1	65	59	0.998604	0.998149	0.208	63	0.9964	0.996261	0.269
mir-8-der	0									
mir-8-dgr	0									
mir-8-dme	0									
mir-8-dmo	–									
mir-8-dpe	0									
mir-8-dps	0									
mir-8-dse	1	68	57	0.998847	0.998842	0.566	65	0.997311	0.997131	0.213
mir-8-dsi	0									
mir-8-dvi	0									
mir-8-dwi	–									
mir-8-dya	0									
mir-9a-dan	0									
mir-9a-der	0									
mir-9a-dgr	0									
mir-9a-dme	0									
mir-9a-dmo	0									
mir-9a-dpe	0									
mir-9a-dps	0									
mir-9a-dse	0									
mir-9a-dsi	0									
mir-9a-dvi	0									
mir-9a-dwi	1	71	62	0.998487	0.998487	0.563	64	0.999074	0.999028	0.521
mir-9b-dan	–									
mir-9b-der	–									
mir-9b-dgr	4	1000	820	0.999512	0.998999	0.679	766	0.999174	0.99791	0.222
mir-9b-dme	3	1000	576	0.999581	0.999403	0.417	751	0.998989	0.998375	0.261
mir-9b-dmo	2	3051	1183	0.999512	0.999536	0.778	1239	0.999169	0.998938	0.263
mir-9b-dpe	0									
mir-9b-dps	0									
mir-9b-dse	–									
mir-9b-dvi	0									
mir-9b-dya	1	77	61	0.999656	0.999656	0.773	71	0.998739	0.998917	0.818
mir-9c-dan	1	79	69	0.998558	0.998345	0.184	74	0.996274	0.995806	0.127
mir-9c-der	0									
mir-9c-dgr	2	606	551	0.996756	0.99668	0.301	544	0.993476	0.997228	0.618
mir-9c-dme	0									
mir-9c-dmo	2	74	67	0.998629	0.998635	0.845	69	0.998023	0.996822	0.561
mir-9c-dpe	0									
mir-9c-dps	0									
mir-9c-dse	0									
mir-9c-dvi	1	77	70	0.998629	0.988029	0.006	71	0.998025	0.996872	0.091
mir-9c-dya	0									
mir-10-dan	1	59	54	0.997733	0.997726	0.449	54	0.99764	0.997522	0.271
mir-10-der	1	59	54	0.997733	0.997696	0.381	58	0.997639	0.99727	0.119
mir-10-dgr	0									

6

micro-RNA	Sub	Samp	Mutational Robustness				Environmental Robustness			
			Uniq	Anc	Desc	Quant	Uniq	Anc	Desc	Quant
mir-10-dme	0									
mir-10-dmo	3	1000	680	0.997741	0.998462	0.451	639	0.99874	0.999129	0.409
mir-10-dpe	0									
mir-10-dps	0									
mir-10-dse	0									
mir-10-dsi	0									
mir-10-dvi	3	1000	786	0.997741	0.998515	0.941	832	0.998739	0.999043	0.897
mir-10-dwi	—									
mir-10-dya	1	59	54	0.997733	0.997726	0.449	57	0.997642	0.997521	0.254
mir-11-dan	13	0	0	0.99623	0.996221	—	0	0.99784	0.996172	—
mir-11-der	2	465	373	0.997611	0.996937	0.271	386	0.999501	0.998451	0.353
mir-11-dgr	—									
mir-11-dme	0									
mir-11-dmo	4	1000	962	0.992076	0.995974	0.522	946	0.992164	0.993662	0.275
mir-11-dpe	0									
mir-11-dps	0									
mir-11-dse	0									
mir-11-dsi	0									
mir-11-dvi	0									
mir-11-dwi	—									
mir-11-dya	0									
mir-12-dan	1	61	54	0.998806	0.998967	0.861	53	0.997805	0.998154	0.852
mir-12-der	1	61	53	0.998806	0.998767	0.500	54	0.997808	0.997692	0.295
mir-12-dgr	0									
mir-12-dme	0									
mir-12-dmo	1	62	55	0.998825	0.998825	0.605	56	0.998153	0.998161	0.677
mir-12-dpe	0									
mir-12-dps	0									
mir-12-dse	0									
mir-12-dsi	0									
mir-12-dvi	0									
mir-12-dwi	0									
mir-13a-dan	1	64	55	0.998815	0.998917	0.883	63	0.999028	0.999031	0.578
mir-13a-der	0									
mir-13a-dgr	3	213	6	0.997626	0.994338	0.357	102	0.997886	0.992424	0.019
mir-13a-dme	0									
mir-13a-dmo	1	59	56	0.997626	0.997769	0.839	57	0.997886	0.998151	0.881
mir-13a-dpe	0									
mir-13a-dps	0									
mir-13a-dse	0									
mir-13a-dsi	0									
mir-13a-dvi	1	59	56	0.997626	0.997605	0.398	59	0.997884	0.997803	0.322
mir-13a-dwi	—									
mir-13a-dya	1	10	10	0.998218	0.998979	0.750	10	0.99837	0.999431	0.700
mir-13b-1-dan	2	51	51	0.995893	0.994	0.814	50	0.995415	0.994567	0.824
mir-13b-1-der	0									
mir-13b-1-dgr	0									
mir-13b-1-dme	1	50	48	0.996639	0.996436	0.330	50	0.995177	0.995779	0.700
mir-13b-1-dmo	5	1000	888	0.996944	0.997907	0.730	954	0.992243	0.996392	0.608
mir-13b-1-dpe	0									
mir-13b-1-dps	0									
mir-13b-1-dse	0									
mir-13b-1-dsi	0									
mir-13b-1-dvi	0									
mir-13b-1-dwi	—									

micro-RNA	Sub	Samp	Mutational Robustness				Environmental Robustness			
			Uniq	Anc	Desc	Quant	Uniq	Anc	Desc	Quant
mir-13b-1-dya	0									
mir-13b-2-dan	–									
mir-13b-2-der	3	1000	856	0.994914	0.994966	0.576	901	0.991738	0.991056	0.259
mir-13b-2-dgr	4	1000	874	0.997119	0.998871	0.946	856	0.998876	0.99936	0.966
mir-13b-2-dme	–									
mir-13b-2-dmo	–									
mir-13b-2-dpe	–									
mir-13b-2-dps	0									
mir-13b-2-dse	0									
mir-13b-2-dsi	0									
mir-13b-2-dvi	3	1000	727	0.997119	0.996046	0.501	897	0.998878	0.9969	0.804
mir-13b-2-dwi	–									
mir-13b-2-dya	1	56	49	0.994914	0.994916	0.616	51	0.99174	0.991729	0.554
mir-14-dan	0									
mir-14-der	0									
mir-14-dgr	0									
mir-14-dme	0									
mir-14-dmo	1	56	48	0.998476	0.997384	0.170	46	0.999385	0.998784	0.054
mir-14-dpe	0									
mir-14-dps	0									
mir-14-dse	0									
mir-14-dsi	0									
mir-14-dvi	0									
mir-14-dwi	1	4	4	0.998476	0.998382	0.375	4	0.999386	0.999529	0.625
mir-14-dya	0									
mir-31a-dan	5	690	636	0.995558	0.997459	0.790	649	0.99201	0.998077	0.827
mir-31a-der	2	65	63	0.996444	0.989186	0.254	51	0.997293	0.999658	0.800
mir-31a-dgr	–									
mir-31a-dme	0									
mir-31a-dmo	–									
mir-31a-dpe	0									
mir-31a-dps	0									
mir-31a-dse	0									
mir-31a-dsi	0									
mir-31a-dvi	1	64	63	0.987724	0.988342	0.648	64	0.993934	0.993912	0.469
mir-31a-dwi	–									
mir-31a-dya	2	132	119	0.996444	0.990359	0.178	124	0.997298	0.997674	0.629
mir-31b-dan	–									
mir-31b-der	0									
mir-31b-dgr	–									
mir-31b-dme	3	1000	943	0.994547	0.986224	0.069	961	0.994221	0.986593	0.162
mir-31b-dmo	–									
mir-31b-dpe	–									
mir-31b-dps	0									
mir-31b-dse	0									
mir-31b-dsi	0									
mir-31b-dvi	–									
mir-31b-dwi	–									
mir-31b-dya	3	1000	946	0.995563	0.991719	0.238	939	0.99536	0.992949	0.290
mir-33-dan	–									
mir-33-der	0									
mir-33-dgr	–									
mir-33-dme	–									
mir-33-dmo	7	1000	931	0.996741	0.997822	0.617	928	0.998246	0.998571	0.809
mir-33-dpe	–									

micro-RNA	Sub	Samp	Uniq	Anc	Desc	Quant	Uniq	Anc	Desc	Quant
				Mutational Robustness				Environmental Robustness		
mir-33-dps	1	83	71	0.997739	0.997738	0.584	79	0.997084	0.997074	0.488
mir-33-dse	0									
mir-33-dsi	0									
mir-33-dvi	−									
mir-33-dwi	−									
mir-33-dya	1	73	60	0.998821	0.998705	0.473	61	0.999233	0.999228	0.610
mir-34-dan	−									
mir-34-der	5	125	123	0.998047	0.996201	0.832	119	0.997109	0.998113	0.960
mir-34-dgr	1	52	47	0.9979	0.996613	0.337	49	0.998176	0.998141	0.404
mir-34-dme	0									
mir-34-dmo	2	956	845	0.9979	0.99836	0.849	762	0.99817	0.998581	0.830
mir-34-dpe	−									
mir-34-dps	0									
mir-34-dse	0									
mir-34-dsi	0									
mir-34-dvi	0									
mir-34-dwi	−									
mir-34-dya	0									
mir-79-dan	−									
mir-79-der	0									
mir-79-dgr	−									
mir-79-dme	−									
mir-79-dmo	−									
mir-79-dpe	−									
mir-79-dps	0									
mir-79-dse	−									
mir-79-dvi	1	82	73	0.999059	0.998967	0.213	66	0.999124	0.999125	0.610
mir-79-dya	1	87	69	0.999314	0.997022	0.006	74	0.99913	0.998986	0.138
mir-87-dan	−									
mir-87-der	0									
mir-87-dgr	0									
mir-87-dme	−									
mir-87-dmo	2	10	10	0.996012	0.996235	0.650	10	0.993814	0.991281	0.600
mir-87-dpe	−									
mir-87-dps	0									
mir-87-dse	0									
mir-87-dsi	0									
mir-87-dvi	2	27	27	0.996012	0.996664	0.685	27	0.99381	0.993667	0.648
mir-87-dya	4	1000	946	0.996785	0.996274	0.868	950	0.994591	0.993694	0.722
mir-92a-dan	−									
mir-92a-der	0									
mir-92a-dgr	−									
mir-92a-dme	0									
mir-92a-dmo	3	1000	846	0.999	0.999165	0.990	881	0.997487	0.998787	0.959
mir-92a-dpe	−									
mir-92a-dps	1	97	86	0.997894	0.997914	0.716	96	0.996057	0.995134	0.165
mir-92a-dse	0									
mir-92a-dsi	0									
mir-92a-dvi	−									
mir-92a-dwi	−									
mir-92a-dya	1	72	60	0.998974	0.998929	0.465	63	0.998622	0.998922	0.986
mir-92b-dan	−									
mir-92b-der	0									
mir-92b-dgr	1	62	53	0.995909	0.995905	0.411	61	0.995986	0.996127	0.694
mir-92b-dme	2	6	6	0.996849	0.99686	0.417	6	0.991051	0.994287	0.500

micro-RNA	Sub	Samp	Mutational Robustness				Environmental Robustness			
			Uniq	Anc	Desc	Quant	Uniq	Anc	Desc	Quant
mir-92b-dmo	0									
mir-92b-dpe	–									
mir-92b-dps	0									
mir-92b-dse	0									
mir-92b-dsi	0									
mir-92b-dvi	1	2	2	0.995909	0.996536	0.250	2	0.995975	0.995154	0.000
mir-92b-dwi	7	0	0	0.995246	0.996559	—	0	0.997078	0.993696	—
mir-92b-dya	0									
mir-100-dan	–									
mir-100-der	0									
mir-100-dgr	1	76	69	0.997432	0.997302	0.375	72	0.998462	0.998473	0.717
mir-100-dme	0									
mir-100-dmo	0									
mir-100-dps	1	2	2	0.986035	0.993409	0.250	2	0.992355	0.993557	0.500
mir-100-dse	0									
mir-100-dsi	0									
mir-100-dvi	0									
mir-100-dwi	0									
mir-100-dya	0									
mir-124-dan	0									
mir-124-der	0									
mir-124-dgr	–									
mir-124-dme	–									
mir-124-dmo	0									
mir-124-dpe	–									
mir-124-dps	0									
mir-124-dse	0									
mir-124-dsi	0									
mir-124-dvi	0									
mir-124-dwi	–									
mir-124-dya	0									
mir-125-dan	0									
mir-125-der	0									
mir-125-dme	0									
mir-125-dmo	0									
mir-125-dps	0									
mir-125-dse	0									
mir-125-dsi	0									
mir-125-dvi	0									
mir-125-dwi	0									
mir-125-dya	0									
mir-133-dan	–									
mir-133-der	–									
mir-133-dgr	2	2473	1678	0.996496	0.995172	0.247	1771	0.996234	0.993128	0.128
mir-133-dme	–									
mir-133-dmo	–									
mir-133-dpe	–									
mir-133-dps	0									
mir-133-dse	0									
mir-133-dsi	0									
mir-133-dvi	4	1000	941	0.996354	0.99313	0.237	918	0.996222	0.989908	0.096
mir-133-dwi	–									
mir-133-dya	0									
mir-184-dan	–									
mir-184-der	0									

micro-RNA	Sub	Samp	Mutational Robustness				Environmental Robustness			
			Uniq	Anc	Desc	Quant	Uniq	Anc	Desc	Quant
mir-184-dgr	–									
mir-184-dme	1	78	75	0.994969	0.994993	0.558	76	0.994924	0.994756	0.423
mir-184-dmo	1	4	4	0.994323	0.996945	0.125	4	0.998456	0.9936	0.250
mir-184-dpe	–									
mir-184-dps	0									
mir-184-dse	0									
mir-184-dsi	0									
mir-184-dvi	0									
mir-184-dwi	–									
mir-184-dya	–									
mir-210-dan	–									
mir-210-der	0									
mir-210-dgr	–									
mir-210-dme	–									
mir-210-dmo	2	222	193	0.996383	0.996535	0.052	190	0.995623	0.997559	0.180
mir-210-dpe	–									
mir-210-dps	0									
mir-210-dse	0									
mir-210-dsi	0									
mir-210-dvi	–									
mir-210-dwi	1	74	72	0.994133	0.996324	0.899	73	0.995357	0.99511	0.311
mir-210-dya	1	74	69	0.993343	0.99657	0.912	72	0.995041	0.995098	0.595
mir-219-dan	–									
mir-219-der	0									
mir-219-dgr	–									
mir-219-dme	0									
mir-219-dmo	–									
mir-219-dpe	–									
mir-219-dps	0									
mir-219-dse	1	72	62	0.997663	0.998076	0.951	72	0.991794	0.992426	0.708
mir-219-dsi	0									
mir-219-dvi	1	6	5	0.996158	0.996164	0.833	6	0.992952	0.992955	0.333
mir-219-dwi	1	4	4	0.997931	0.997908	0.875	4	0.994261	0.99372	0.750
mir-219-dya	0									
mir-263a-dan	–									
mir-263a-der	1	1	1	0.997731	0.997247	0.500	1	0.995038	0.994447	0.000
mir-263a-dgr	1	71	63	0.997247	0.997222	0.444	71	0.992668	0.992606	0.324
mir-263a-dme	–									
mir-263a-dmo	1	71	63	0.997247	0.997247	0.542	66	0.99267	0.992658	0.408
mir-263a-dpe	–									
mir-263a-dps	0									
mir-263a-dse	1	86	72	0.997732	0.997919	0.855	84	0.994509	0.995398	0.826
mir-263a-dsi	0									
mir-263a-dvi	1	71	63	0.997247	0.997247	0.542	66	0.992659	0.992676	0.549
mir-263a-dwi	–									
mir-263a-dya	0									
mir-263b-dan	–									
mir-263b-der	–									
mir-263b-dgr	2	384	261	0.998434	0.998688	0.970	318	0.998307	0.998728	0.917
mir-263b-dme	0									
mir-263b-dpe	1	5	5	0.998475	0.998236	0.100	5	0.996206	0.994773	0.200
mir-263b-dps	–									
mir-263b-dse	0									
mir-263b-dsi	0									
mir-263b-dvi	–									

micro-RNA	Sub	Samp	Mutational Robustness				Environmental Robustness			
			Uniq	Anc	Desc	Quant	Uniq	Anc	Desc	Quant
mir-263b-dwi	–									
mir-274-dan	–									
mir-274-der	0									
mir-274-dgr	–									
mir-274-dme	1	75	61	0.999082	0.999048	0.313	56	0.99918	0.999121	0.207
mir-274-dmo	–									
mir-274-dpe	–									
mir-274-dps	0									
mir-274-dse	–									
mir-274-dvi	2	76	63	0.998025	0.992638	0.059	69	0.996582	0.994549	0.145
mir-274-dwi	–									
mir-274-dya	1	66	57	0.998994	0.999458	0.902	53	0.999128	0.999145	0.833
mir-275-dan	–									
mir-275-der	0									
mir-275-dgr	2	455	415	0.996477	0.996384	0.499	417	0.998087	0.998199	0.651
mir-275-dme	–									
mir-275-dmo	3	1000	919	0.996477	0.996779	0.599	916	0.998081	0.998993	0.943
mir-275-dpe	–									
mir-275-dps	0									
mir-275-dse	1	3	3	0.999298	0.998698	0.167	3	0.99951	0.998306	0.167
mir-275-dsi	0									
mir-275-dvi	2	83	75	0.996477	0.995685	0.590	77	0.998087	0.997866	0.578
mir-275-dwi	–									
mir-275-dya	1	95	79	0.999274	0.999274	0.663	73	0.999647	0.999647	0.600
mir-276a-dan	–									
mir-276a-der	0									
mir-276a-dgr	3	1000	573	0.99883	0.998654	0.505	707	0.999025	0.998045	0.293
mir-276a-dme	–									
mir-276a-dmo	1	86	68	0.99883	0.998832	0.605	70	0.999024	0.999126	0.785
mir-276a-dpe	0									
mir-276a-dps	–									
mir-276a-dse	0									
mir-276a-dsi	0									
mir-276a-dvi	0									
mir-276a-dwi	1	87	72	0.998746	0.998746	0.489	75	0.99881	0.998805	0.466
mir-276a-dya	0									
mir-276b-dan	–									
mir-276b-der	0									
mir-276b-dgr	1	98	80	0.998617	0.998913	0.883	80	0.999367	0.999385	0.755
mir-276b-dme	–									
mir-276b-dmo	1	98	79	0.998402	0.998252	0.281	90	0.999397	0.999286	0.286
mir-276b-dpe	–									
mir-276b-dps	0									
mir-276b-dse	0									
mir-276b-dsi	0									
mir-276b-dvi	1	98	79	0.998402	0.998269	0.301	87	0.999397	0.99934	0.337
mir-276b-dwi	2	4814	1026	0.999271	0.999376	0.904	1202	0.999528	0.99954	0.743
mir-276b-dya	0									
mir-277-dan	–									
mir-277-der	0									
mir-277-dgr	0									
mir-277-dme	0									
mir-277-dmo	–									
mir-277-dpe	–									
mir-277-dps	0									

micro-RNA	Sub	Samp	Mutational Robustness				Environmental Robustness			
			Uniq	Anc	Desc	Quant	Uniq	Anc	Desc	Quant
mir-277-dse	0									
mir-277-dsi	4	1000	678	0.999055	0.995998	0.020	803	0.998425	0.996959	0.080
mir-277-dvi	0									
mir-277-dwi	3	1000	565	0.999263	0.99929	0.832	705	0.998088	0.998309	0.849
mir-277-dya	0									
mir-278-dan	–									
mir-278-der	0									
mir-278-dgr	3	1000	387	0.997247	0.997201	0.821	788	0.997139	0.996354	0.235
mir-278-dme	1	89	78	0.99713	0.997478	0.921	89	0.994758	0.99479	0.551
mir-278-dmo	–									
mir-278-dpe	–									
mir-278-dps	0									
mir-278-dse	0									
mir-278-dsi	0									
mir-278-dvi	1	76	69	0.997155	0.99579	0.086	74	0.997097	0.997266	0.704
mir-278-dwi	4	1000	775	0.997802	0.997926	0.391	861	0.996728	0.996888	0.228
mir-278-dya	0									
mir-279-dan	–									
mir-279-der	0									
mir-279-dgr	–									
mir-279-dme	–									
mir-279-dmo	2	5	5	0.996784	0.997223	0.900	5	0.993873	0.996009	0.900
mir-279-dpe	–									
mir-279-dps	0									
mir-279-dse	0									
mir-279-dsi	0									
mir-279-dvi	–									
mir-279-dwi	–									
mir-279-dya	2	2957	1550	0.994942	0.99617	0.728	2392	0.988585	0.994806	0.687
mir-280-dan	–									
mir-280-der	1	2	2	0.992234	0.993103	0.750	2	0.989894	0.99287	0.000
mir-280-dgr	–									
mir-280-dme	1	78	70	0.993286	0.986859	0.071	77	0.986668	0.982474	0.103
mir-280-dmo	2	8	8	0.994258	0.997058	0.812	8	0.990724	0.996248	0.875
mir-280-dpe	–									
mir-280-dps	0									
mir-280-dse	–									
mir-280-dvi	–									
mir-280-dwi	–									
mir-280-dya	–									
mir-281-1-dan	–									
mir-281-1-der	0									
mir-281-1-dgr	1	1	1	0.998413	0.997959	0.500	1	0.996996	0.997081	0.000
mir-281-1-dme	1	80	72	0.9992	0.999185	0.581	78	0.998313	0.998207	0.312
mir-281-1-dmo	2	2453	1330	0.998619	0.998558	0.632	1684	0.99812	0.998171	0.714
mir-281-1-dpe	0									
mir-281-1-dps	0									
mir-281-1-dse	0									
mir-281-1-dvi	2	11	11	0.998619	0.997987	0.591	11	0.99812	0.996371	0.727
mir-281-1-dwi	5	1000	791	0.998468	0.998722	0.769	901	0.996252	0.997747	0.685
mir-281-1-dya	2	3304	1352	0.9992	0.999138	0.608	1641	0.998312	0.997792	0.252
mir-281-2-dan	1	10	10	0.995786	0.996555	0.550	10	0.994172	0.994633	0.500
mir-281-2-der	0									
mir-281-2-dgr	1	73	69	0.998487	0.998579	0.801	66	0.998849	0.998997	0.877
mir-281-2-dme	0									

micro-RNA	Sub	Samp	Mutational Robustness				Environmental Robustness			
			Uniq	Anc	Desc	Quant	Uniq	Anc	Desc	Quant
mir-281-2-dmo	2	19	19	0.998487	0.998049	0.500	19	0.998852	0.995247	0.211
mir-281-2-dpe	0									
mir-281-2-dps	0									
mir-281-2-dse	0									
mir-281-2-dvi	–									
mir-281-2-dwi	–									
mir-281-2-dya	3	1000	789	0.997388	0.998122	0.914	843	0.993896	0.994452	0.552
mir-282-dan	–									
mir-282-der	1	5	4	0.998846	0.999258	0.800	5	0.99812	0.999142	0.200
mir-282-dgr	–									
mir-282-dme	1	75	61	0.998597	0.998834	0.913	71	0.997349	0.998337	0.933
mir-282-dmo	–									
mir-282-dpe	–									
mir-282-dps	0									
mir-282-dse	1	75	61	0.998597	0.998496	0.293	71	0.997346	0.99626	0.067
mir-282-dsi	0									
mir-282-dvi	1	80	68	0.99902	0.998261	0.019	73	0.997994	0.996758	0.087
mir-282-dwi	–									
mir-282-dya	–									
mir-283-dan	–									
mir-283-der	0									
mir-283-dgr	–									
mir-283-dme	–									
mir-283-dmo	–									
mir-283-dpe	–									
mir-283-dps	0									
mir-283-dse	0									
mir-283-dsi	0									
mir-283-dvi	0									
mir-283-dwi	–									
mir-283-dya	0									
mir-284-dan	–									
mir-284-der	0									
mir-284-dgr	2	146	132	0.978105	0.96369	0.469	143	0.983019	0.968075	0.219
mir-284-dme	1	76	63	0.991134	0.993837	0.941	74	0.983973	0.989077	0.934
mir-284-dmo	5	690	672	0.978105	0.958677	0.022	667	0.982991	0.968311	0.016
mir-284-dpe	–									
mir-284-dps	0									
mir-284-dse	0									
mir-284-dsi	0									
mir-284-dvi	1	2	2	0.978105	0.972221	0.250	2	0.983015	0.969783	0.250
mir-284-dwi	–									
mir-284-dya	0									
mir-285-dan	–									
mir-285-der	3	1000	618	0.998715	0.99842	0.818	823	0.996955	0.996489	0.713
mir-285-dgr	–									
mir-285-dme	2	206	159	0.998518	0.998649	0.488	191	0.996263	0.998091	0.631
mir-285-dmo	–									
mir-285-dps	6	1000	819	0.998633	0.997138	0.141	929	0.998417	0.993222	0.107
mir-285-dse	1	89	70	0.998472	0.998014	0.051	83	0.99619	0.995636	0.169
mir-285-dsi	0									
mir-285-dvi	3	1000	727	0.998311	0.998071	0.278	858	0.9968	0.995816	0.372
mir-285-dwi	–									
mir-285-dya	1	100	75	0.998715	0.998724	0.685	95	0.99696	0.997354	0.820
mir-286-dan	–									

micro-RNA	Sub	Samp	Uniq	Mutational Robustness Anc	Desc	Quant	Uniq	Environmental Robustness Anc	Desc	Quant
mir-286-der	2	1	1	0.991552	0.98807	0.500	1	0.990662	0.981107	1.000
mir-286-dme	–									
mir-286-dmo	6	1000	931	0.99518	0.997731	0.674	954	0.992827	0.993928	0.527
mir-286-dpe	–									
mir-286-dps	0									
mir-286-dse	–									
mir-286-dsi	0									
mir-286-dvi	–									
mir-286-dwi	–									
mir-286-dya	1	77	76	0.991552	0.9868	0.058	76	0.990662	0.98337	0.026
mir-287-dan	–									
mir-287-der	5	0	0	0.911064	0.925945	—	0	0.968225	0.977545	—
mir-287-dme	–									
mir-287-dmo	–									
mir-287-dpe	–									
mir-287-dps	0									
mir-287-dse	0									
mir-287-dsi	0									
mir-287-dvi	0									
mir-287-dwi	7	647	645	0.936672	0.961715	0.434	639	0.961749	0.965901	0.258
mir-287-dya	–									
mir-288-dan	–									
mir-288-der	2	2	2	0.93708	0.917895	0.250	2	0.986905	0.950597	0.000
mir-288-dgr	–									
mir-288-dme	2	2922	2884	0.921466	0.899049	0.157	2863	0.957292	0.942928	0.182
mir-288-dmo	–									
mir-288-dpe	1	11	11	0.995442	0.99507	0.409	11	0.996643	0.997159	1.000
mir-288-dps	0									
mir-288-dse	0									
mir-288-dsi	0									
mir-288-dvi	2	10	10	0.977506	0.904057	0.950	10	0.991792	0.948236	0.900
mir-288-dwi	–									
mir-288-dya	–									
mir-289-dan	–									
mir-289-der	2	3	3	0.994721	0.995221	0.833	3	0.99791	0.996921	0.667
mir-289-dme	1	1	1	0.995074	0.988699	0.500	1	0.997846	0.982899	0.500
mir-289-dpe	–									
mir-289-dps	0									
mir-289-dse	0									
mir-289-dsi	0									
mir-289-dya	2	4	4	0.994721	0.981842	0.875	4	0.997906	0.991199	1.000
mir-304-dan	2	61	59	0.995973	0.982074	0.074	61	0.995568	0.994567	0.377
mir-304-der	0									
mir-304-dgr	2	74	70	0.996514	0.997129	0.885	73	0.995565	0.994552	0.635
mir-304-dme	1	65	61	0.996823	0.996396	0.177	63	0.998165	0.997298	0.200
mir-304-dmo	2	2139	1697	0.996513	0.996814	0.798	1737	0.995772	0.996158	0.703
mir-304-dps	4	1000	945	0.995973	0.995547	0.506	917	0.995569	0.997884	0.884
mir-304-dse	0									
mir-304-dsi	0									
mir-304-dvi	1	2	2	0.996513	0.997689	0.750	2	0.995771	0.9971	0.500
mir-304-dwi	8	0	0	0.990366	0.995368	—	0	0.995493	0.995763	—
mir-304-dya	0									
mir-305-dan	1	53	51	0.996724	0.996315	0.462	52	0.996504	0.995141	0.264
mir-305-der	1	47	46	0.99564	0.990908	0.330	47	0.992683	0.993501	0.809
mir-305-dgr	0									

| micro-RNA | Sub | Samp | Uniq | Mutational Robustness | | | Uniq | Environmental Robustness | | |
				Anc	Desc	Quant		Anc	Desc	Quant
mir-305-dme	0									
mir-305-dmo	3	1000	771	0.996805	0.995346	0.208	798	0.99592	0.99634	0.167
mir-305-dpe	0									
mir-305-dps	0									
mir-305-dse	0									
mir-305-dsi	–									
mir-305-dvi	1	3	3	0.996805	0.996622	0.500	3	0.995922	0.993843	0.333
mir-305-dwi	–									
mir-305-dya	0									
mir-306-dan	10	0	0	0.998181	0.998441	—	0	0.997613	0.998444	—
mir-306-der	0									
mir-306-dgr	–									
mir-306-dme	0									
mir-306-dmo	–									
mir-306-dpe	0									
mir-306-dps	0									
mir-306-dse	–									
mir-306-dvi	3	1000	541	0.999224	0.998948	0.237	734	0.999076	0.998908	0.489
mir-306-dya	1	2	2	0.998008	0.998929	0.250	2	0.996801	0.998559	0.500
mir-307-dan	0									
mir-307-der	0									
mir-307-dgr	0									
mir-307-dme	0									
mir-307-dmo	1	1	1	0.9971	0.997866	0.500	1	0.994734	0.994217	1.000
mir-307-dpe	0									
mir-307-dps	0									
mir-307-dse	0									
mir-307-dsi	0									
mir-307-dvi	1	6	6	0.9971	0.995809	0.417	6	0.994738	0.993918	0.167
mir-307-dwi	–									
mir-307-dya	0									
mir-308-dan	–									
mir-308-der	1	2	2	0.993205	0.992048	0.250	2	0.996502	0.993014	0.500
mir-308-dgr	0									
mir-308-dme	2	88	85	0.993205	0.995202	0.562	86	0.996497	0.998079	0.875
mir-308-dmo	2	989	715	0.995847	0.996344	0.926	822	0.995076	0.995387	0.644
mir-308-dpe	0									
mir-308-dps	0									
mir-308-dse	0									
mir-308-dsi	0									
mir-308-dvi	1	43	38	0.995847	0.993445	0.105	42	0.995071	0.994966	0.349
mir-308-dwi	5	1000	952	0.994849	0.995887	0.643	957	0.996837	0.997061	0.755
mir-308-dya	1	4	4	0.993205	0.995177	0.875	4	0.996492	0.996009	0.750
mir-309-dan	0									
mir-309-der	0									
mir-309-dme	0									
mir-309-dmo	3	1000	692	0.997246	0.997527	0.837	870	0.99645	0.996912	0.739
mir-309-dpe	0									
mir-309-dps	0									
mir-309-dse	0									
mir-309-dsi	0									
mir-309-dvi	–									
mir-309-dwi	–									
mir-309-dya	1	3	3	0.981819	0.974911	0.500	3	0.990971	0.982599	0.333
mir-314-dan	–									

micro-RNA	Sub	Samp	Uniq	Mutational Robustness Anc	Desc	Quant	Uniq	Environmental Robustness Anc	Desc	Quant
mir-314-der	1	84	78	0.997544	0.997194	0.339	80	0.997652	0.997641	0.536
mir-314-dgr	–									
mir-314-dme	3	1000	471	0.997416	0.992612	0.416	914	0.997624	0.993108	0.695
mir-314-dmo	–									
mir-314-dpe	0									
mir-314-dps	0									
mir-314-dse	0									
mir-314-dsi	0									
mir-314-dvi	–									
mir-314-dwi	0									
mir-314-dya	1	1	1	0.997544	0.992386	0.500	1	0.997649	0.989203	0.000
mir-315-dan	4	1000	535	0.999259	0.998396	0.149	708	0.998045	0.996871	0.157
mir-315-der	–									
mir-315-dgr	7	1000	658	0.999408	0.999275	0.644	810	0.999578	0.998781	0.470
mir-315-dme	1	68	54	0.999273	0.999127	0.184	57	0.9995	0.998793	0.029
mir-315-dmo	–									
mir-315-dpe	0									
mir-315-dps	0									
mir-315-dse	–									
mir-315-dsi	0									
mir-315-dwi	–									
mir-316-dan	2	2268	1553	0.998286	0.998568	0.904	1785	0.996999	0.998269	0.924
mir-316-der	1	66	64	0.997998	0.99776	0.326	64	0.997112	0.996094	0.227
mir-316-dgr	–									
mir-316-dme	1	69	67	0.996726	0.998159	0.833	69	0.989549	0.99567	0.754
mir-316-dmo	–									
mir-316-dpe	0									
mir-316-dps	0									
mir-316-dse	0									
mir-316-dsi	0									
mir-316-dvi	0									
mir-316-dwi	4	1000	890	0.998286	0.99872	0.976	934	0.996999	0.998668	0.982
mir-317-dan	4	0	0	0.997208	0.997395	—	0	0.994829	0.995037	—
mir-317-der	0									
mir-317-dgr	–									
mir-317-dme	0									
mir-317-dmo	–									
mir-317-dps	5	1000	965	0.994307	0.993708	0.547	957	0.991852	0.991955	0.463
mir-317-dse	0									
mir-317-dsi	0									
mir-317-dvi	–									
mir-317-dwi	–									
mir-317-dya	0									
mir-318-dan	4	1000	707	0.998565	0.998374	0.329	823	0.997351	0.997011	0.215
mir-318-der	0									
mir-318-dgr	0									
mir-318-dme	0									
mir-318-dmo	1	54	49	0.995833	0.996204	0.806	51	0.993864	0.993874	0.481
mir-318-dpe	0									
mir-318-dps	0									
mir-318-dse	0									
mir-318-dsi	1	65	55	0.999012	0.999342	0.946	57	0.998381	0.998977	0.892
mir-318-dvi	0									
mir-318-dya	2	2149	840	0.999012	0.997752	0.023	1230	0.998379	0.99498	0.024