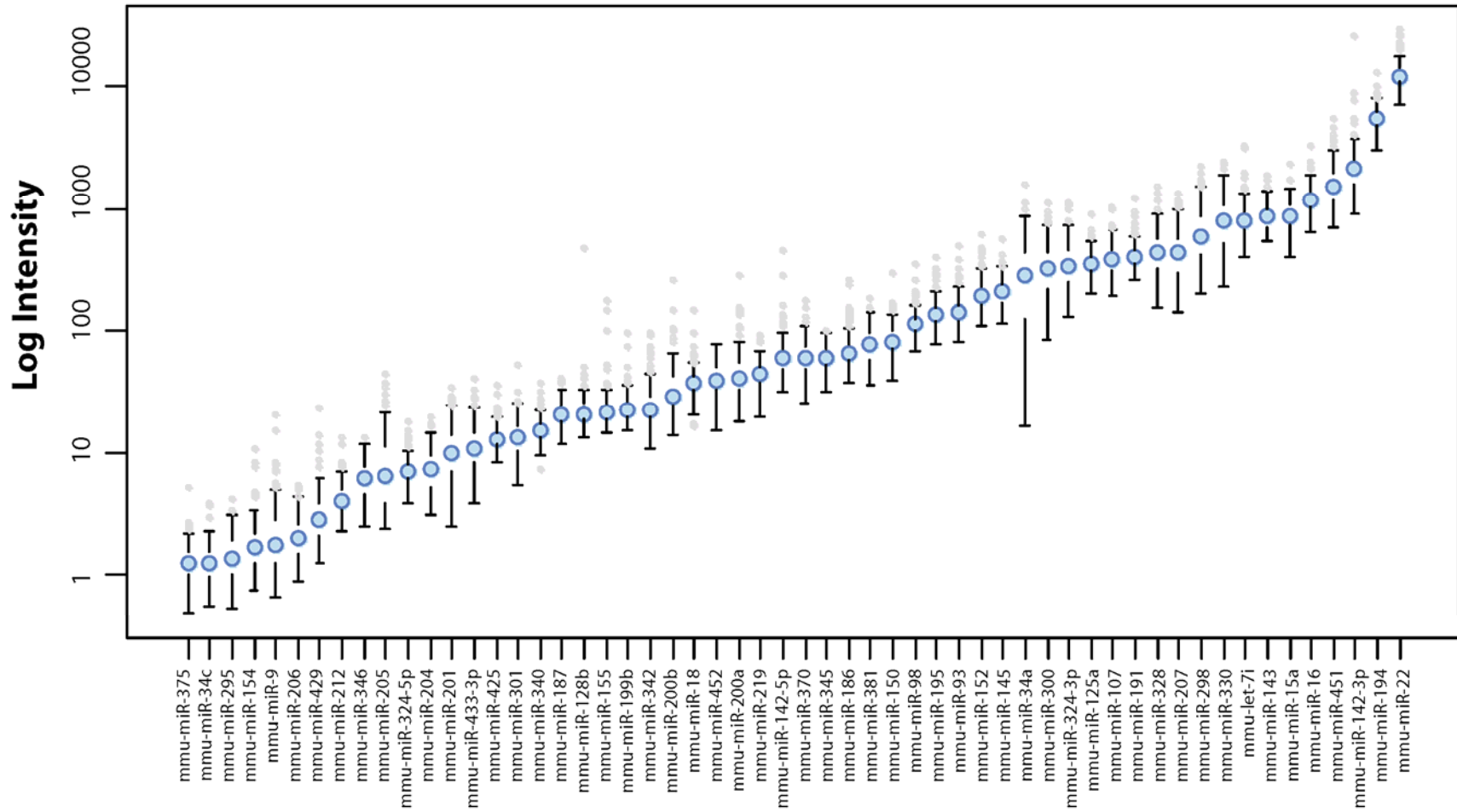
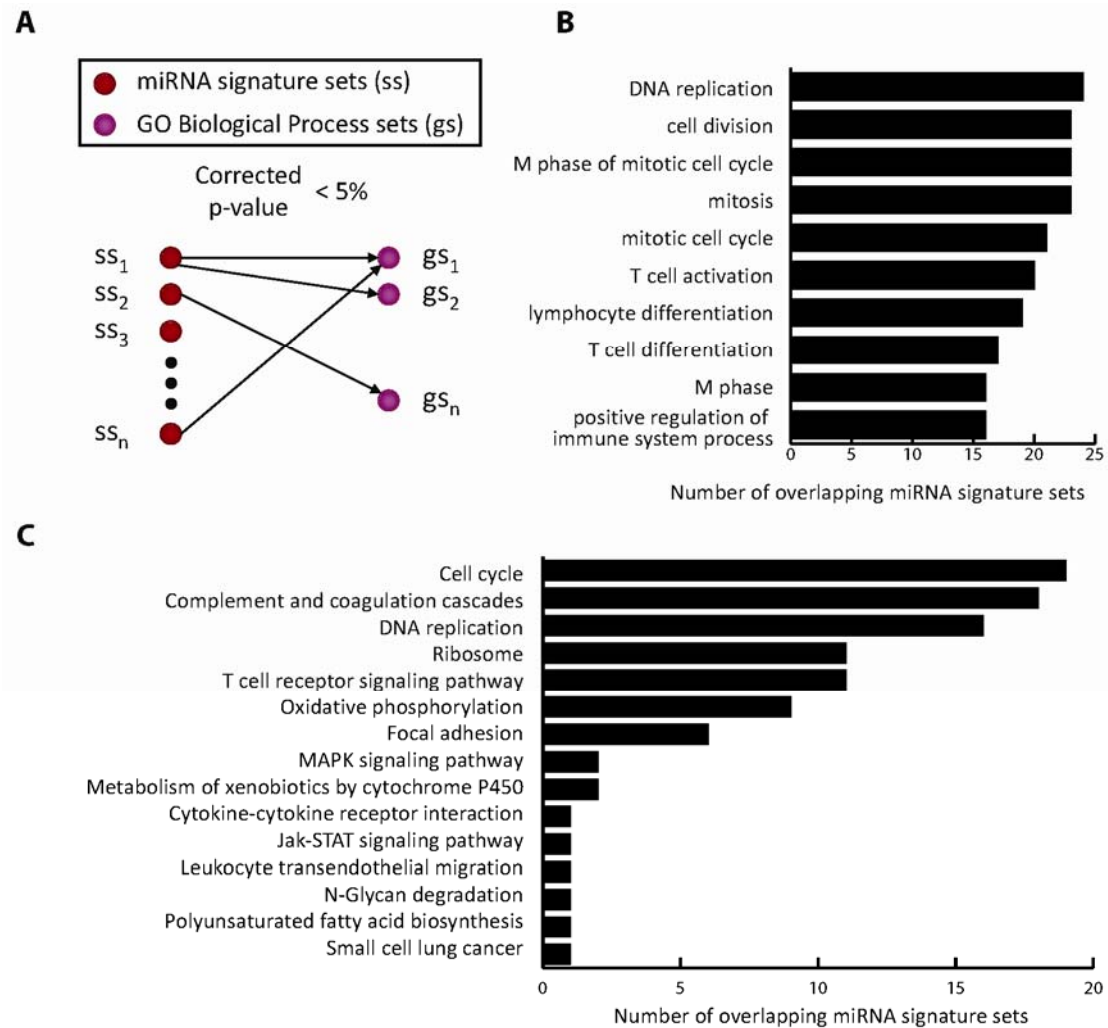


Supplementary figure 1. Distribution of eQTLs in 2 and 20 cM bins for mRNA and miRNA eQTLs, respectively, across the genome at a 10% FDR threshold. Top panel illustrates all mRNA eQTLs with LOD scores > 4.3 while the bottom panel illustrates all miRNA eQTLs with LOD scores > 3.2

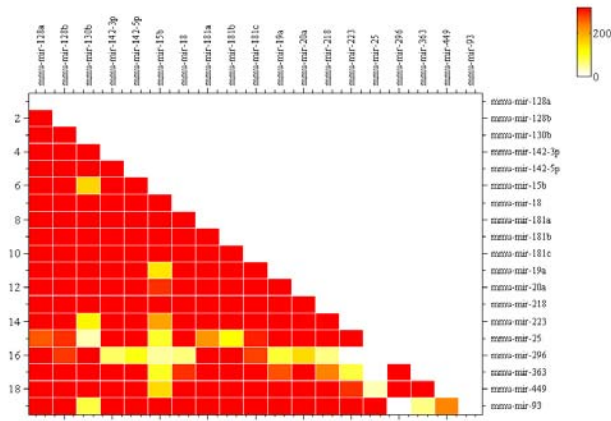


Supplementary figure 2. Intensity measurements for miRNAs with detectable eQTLs (FDR < 10%)

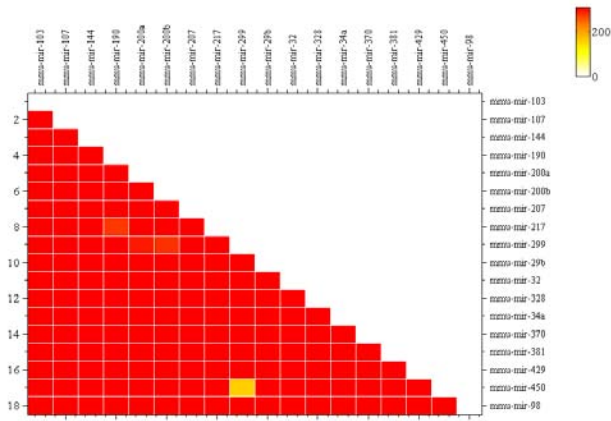


Supplementary figure 3. Summary of miRNA-mRNA correlation analysis. A. Illustration of the enrichment analysis. Fisher's exact test statistics for all pairwise comparisons between each set of miRNA signature sets and each category in GO Biological Process are computed. P-values are corrected for multiple hypothesis testing using a Bonferroni's correction. The same analysis is repeated using sets in KEGG Pathways and Body Atlas Tissue Enrichment databases. Significant enrichment between the sets are defined as those with a corrected p-value of less than 0.05. B. Histogram showing the top 10 categories for GO Biological Process category in terms of number of enriched miRNAs signature sets. C. Histogram showing the number of enriched miRNA signature sets in each KEGG pathway category.

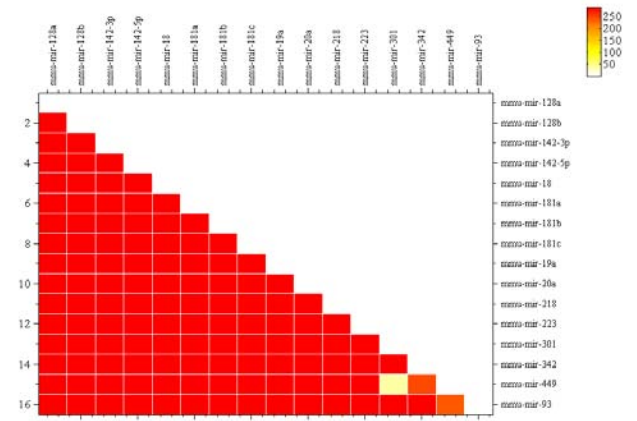
Cell cycle



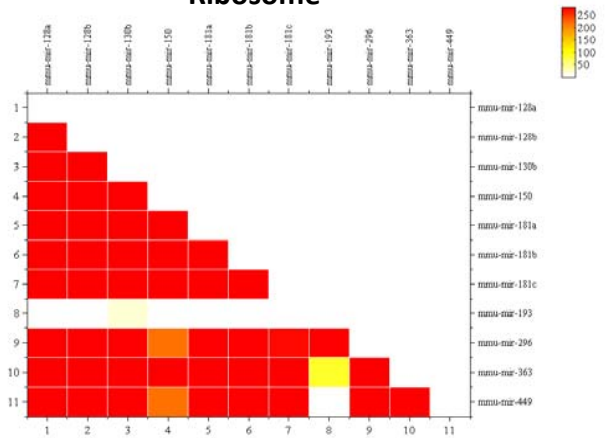
Complement & Coagulation pathway



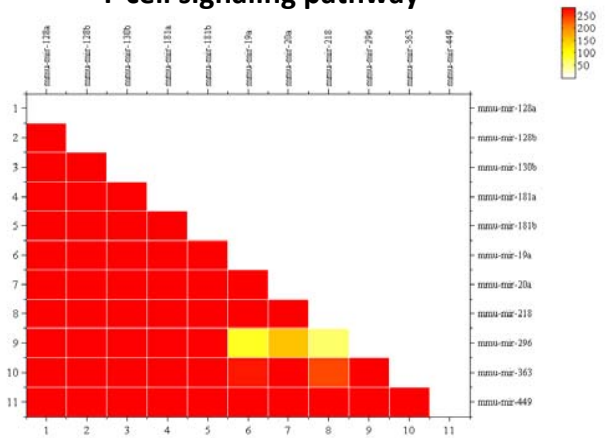
DNA replication



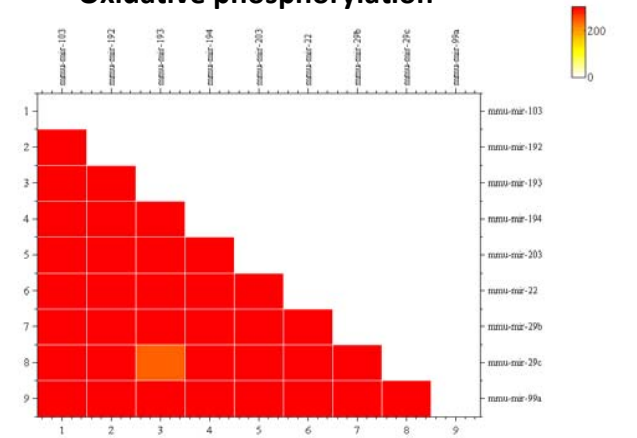
Ribosome



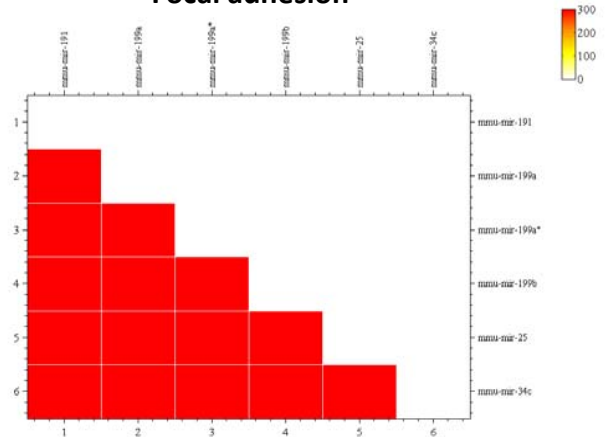
T-cell signaling pathway



Oxidative phosphorylation



Focal adhesion



Supplementary figure 4. Fisher exact test for significant association between two miRNA signature set associated with the same KEGG pathway. $-\log_{10}$ p-values were used to build the heatmap.

Supplementary Table 2. Top 10 results (ordered by enrichment fold-change) for GO Biological Process Enrichment, KEGG Pathways Enrichment

MicroRNA	Category	miRNA signature set size	GO set size	Overlap (Enrichment) ^a	Nominal p-value ^b	Corrected p-value ^b
<i>GO Biological Process</i>						
mmu-mir-92	RNA splicing	431	265	32(4.43)	1.55E-12	1.02E-08
mmu-mir-92	DNA replication	431	216	25(4.25)	1.12E-09	7.35E-06
mmu-mir-130b	chromosome segregation	1434	81	29(3.95)	3.45E-11	2.26E-07
mmu-mir-449	spindle organization and biogenesis	2506	32	20(3.94)	3.03E-09	1.98E-05
mmu-mir-192	oxidative phosphorylation	1334	60	19(3.75)	2.48E-07	1.63E-03
mmu-mir-20a	DNA replication initiation	2962	30	21(3.74)	1.23E-09	8.08E-06
mmu-mir-130b	DNA-dependent DNA replication	1434	77	26(3.72)	1.54E-09	1.01E-05
mmu-mir-449	negative regulation of DNA metabolic process	2506	33	19(3.63)	5.08E-08	3.33E-04
mmu-mir-92	chromatin modification	431	266	26(3.59)	1.89E-08	1.24E-04
mmu-mir-92	mRNA metabolic process	431	318	31(3.58)	8.38E-10	5.49E-06
<i>KEGG Pathways</i>						
mmu-mir-150	Ribosome	543	75	48(4.75)	1.35E-24	2.68E-22
mmu-mir-19a	DNA replication	618	33	23(4.55)	2.58E-12	5.10E-10
mmu-mir-15b	Cell cycle	192	108	23(4.47)	5.56E-10	1.10E-07
mmu-mir-296	Ribosome	470	75	39(4.46)	5.49E-18	1.09E-15
mmu-mir-449	DNA replication	703	33	25(4.35)	2.53E-13	5.02E-11
mmu-mir-193	Ribosome	411	75	30(3.93)	6.63E-12	1.31E-09
mmu-mir-299	Complement and coagulation cascades	344	69	23(3.91)	3.93E-09	7.79E-07
mmu-mir-363	Ribosome	599	75	43(3.86)	9.28E-18	1.84E-15
mmu-mir-29c	Oxidative phosphorylation	312	119	34(3.69)	4.85E-12	9.59E-10
mmu-mir-20a	DNA replication	785	33	23(3.58)	4.29E-10	8.50E-08

^aThe number in the parentheses is the fold-change enrichment. The fold-change enrichment is defined to be the observed overlap divided by the observed overlap.

^bThe nominal p-value represents the Fisher's exact test statistics while the corrected p-value represents the Bonferroni-corrected p-value (nominal p-value multiplied by the number of sets searched).

Supplementary Table 3. Top 10 results (ordered by enrichment fold-change) for miRNA signature sets (significant correlation and at least 1 hexamer seed)

MicroRNA	seed (6mer)	Category	miRNA signature set size	GO set size	Overlap (Enrichment) ^a	Nominal p-value ^b	Corrected p-value ^b
<i>GO Biological Process</i>							
mmu-mir-92	GTGCAA	chromosome organization and biogenesis	168	494	25(4.76)	8.57E-11	5.61E-07
mmu-mir-150	TGGGAG	immune response-regulating cell surface receptor signaling pathway	912	87	18(3.59)	1.86E-06	1.22E-02
mmu-mir-150	TGGGAG	immune response-regulating signal transduction	912	111	22(3.44)	3.02E-07	1.98E-03
mmu-mir-181a	GAATGT	regulation of cell-cell adhesion	2571	31	17(3.37)	9.76E-07	6.39E-03
mmu-mir-150	TGGGAG	immune response-activating signal transduction	912	108	21(3.37)	7.79E-07	5.10E-03
mmu-mir-449	CACTGC	regulation of DNA metabolic process	1255	86	23(3.37)	1.47E-07	9.60E-04
mmu-mir-199a	ACTGGG	positive regulation of cellular component organization and biogenesis	758	134	21(3.27)	1.55E-06	1.02E-02
mmu-mir-130b	TGCACT	DNA replication	608	216	27(3.25)	6.87E-08	4.50E-04
mmu-mir-34c	CACTGC	extracellular structure organization and biogenesis	491	248	25(3.25)	2.38E-07	1.56E-03
mmu-mir-132	CTGTTA	immune response-activating signal transduction	918	108	20(3.19)	3.47E-06	2.27E-02
<i>KEGG Pathways</i>							
mmu-mir-20a	CACTTT	Cell cycle	377	108	33(3.27)	2.50E-10	4.94E-08
mmu-mir-19a	TTGCAC	T cell receptor signaling pathway	306	94	22(3.08)	1.12E-06	2.22E-04
mmu-mir-301	TGCACT	Small cell lung cancer	355	86	23(3.04)	7.00E-07	1.39E-04
mmu-mir-218	AGCACA	T cell receptor signaling pathway	426	94	30(3.02)	1.02E-08	2.02E-06
mmu-mir-301	TGCACT	Pancreatic cancer	355	72	19(3)	8.27E-06	1.64E-03
mmu-mir-429	CAGTAT	Small cell lung cancer	236	86	15(2.98)	1.07E-04	2.12E-02
mmu-mir-449	CACTGC	T cell receptor signaling pathway	342	94	23(2.89)	1.97E-06	3.90E-04
mmu-mir-449	CACTGC	B cell receptor signaling pathway	342	66	16(2.86)	8.39E-05	1.66E-02
mmu-mir-218	AGCACA	Glioma	426	63	19(2.86)	1.41E-05	2.79E-03
mmu-mir-32	GTGCAA	Small cell lung cancer	264	86	16(2.84)	1.08E-04	2.14E-02

^aThe number in the parentheses is the fold-change enrichment. The fold-change enrichment is defined to be the observed overlap divided by the expected overlap.

^bThe nominal p-value represents the Fisher's exact test statistics while the corrected p-value represents the Bonferroni-corrected p-value (nominal p-value multiplied by the number of sets searched).