

Supplementary Methods

RNA Analyses

Human plasma samples: miRNA was extracted from 200µl plasma using Exiqon's miRCURY™ RNA isolation kit for biofluids. Extraction (per manufacturer's instruction) included carrier RNA (MS2) and RNA-spike-in controls to monitor efficiency. RNA was eluted in 50µl. 8µl RNA was reverse transcribed using the miRCURY LNA™ Universal cDNA synthesis kit (Exiqon) and quality assessed for sample purity, cDNA synthesis and haemolysis using the miRCURY™ microRNA QC PCR Panel (Exiqon). All samples passing quality control were run against the Exiqon serum/plasma focus microRNA panel V1 (175 miRNAs) using the miRCURY LNA miRNA PCR ExiLENT SYBR green master mix.

EVs were extracted from 500µl plasma from n=6 individuals with obesity using the exoRNEASy kit (Qiagen), which has a high specificity for EV RNA over non-EV plasma RNA (1). EVs were captured on filter and Trizol extracted (manufacturer's protocol). Flow through was collected ('non-EV fraction') and extracted as per captured EVs. Real-time QRT-PCR (RTqPCR) was performed using Exiqon reagents and specific LNA primers. miRNA were deemed undetectable at a Ct threshold of ≥ 35 .

Mouse plasma and tissue samples: miRNA was isolated using the Exiqon miRCURY™ RNA isolation kit for biofluids (plasma) and tissue as appropriate. RNA (max volume plasma, 500 ng tissue) was reverse transcribed using the miRCURY LNA™ Universal cDNA synthesis kit.

Data analyses

All statistical analyses were performed in R (2).

Human plasma miRNA: Of the 175 miRNA measured, 4 were classified undetectable (miR-297, miR-885-5p, miR-95 and miR-346) with Ct values ≥ 35 in at least 65% of samples. Interplate calibration (IPC) using UniSp3 controls was used to correct for variance across plates. Detectable miRNA were assessed for least variance across all samples and groups,

identifying miR-93 as the miRNA showing least variance and therefore a potential endogenous control. This was confirmed by comparison of the five suggested Exiqon controls using Exiqon software (GenEx v2.5), which identified miR-93 as the best control, and significant variance of the other four potential controls. Furthermore, miR-93 did not vary significantly in plasma in our murine model of obesity (normal chow: mean Ct 18.96 ± 0.65 vs HFHS diet mean Ct 19.05 ± 0.30). Therefore, to avoid additional variance, and because it validated in mouse plasma miR-93 alone was selected as a normalisation control. Each miRNA was normalized using the Δ Ct method (i.e. $Ct_{\text{candidatemiRNA}} - Ct_{\text{miR93}}$). miRNA levels were compared between groups using the Kolmogorov-Smirnov (KS) test, with results corrected for multiple testing (Bonferroni adjusted $P \leq 0.05$ threshold of significance).

Correlations between miRNA level (Δ Ct) and clinical parameters were investigated using Pearson correlation. The clinical data was minimally ragged, with 14 individuals missing data for one clinical variable. Therefore, in order to retain maximum power by not removing individuals from the analysis, missing data were imputed using the imputePCA function in the missMDA (3) package prior to analysis. Correlations with an absolute $r \geq 0.3$ and passing an $FDR \leq 0.05$ threshold were deemed significant. To further investigate these associations stepwise regression analyses (both directions) were performed using the stepAIC function in the MASS package (4) with clinical trait as the response variable against all miRNA for which a significant correlation with that trait was observed. Models with the miRNA expression level as a significant co-variate and an overall model P value of 0.05 were included. Model P values were generated from ANOVA using the F distribution, which tests the null hypothesis that the coefficients represented in the overall regression model (represented by R^2) are equal to 0. We performed a further step-wise regression whereby we added clinical and anthropometric variables (Table 1) to the final miRNA models (Table 5). Variables used to derive the response variable, or with an intrinsic relationship to it, were excluded from the relevant model (i.e McA - BMI, triglycerides, insulin and HOMA-IR excluded, HOMA-IR - insulin, glucose and McA

excluded, insulin - HOMA-IR and McA excluded, glucose – HOMA-IR excluded, triglycerides – McA excluded).

Mouse miRNA analysis

miRNA levels were assayed using Exiqon LNA RTqPCR specific primers with plasma and tissue levels normalised to miR-93 and snRNA U6 respectively using the ΔCt approach ($\text{Ct}_{\text{candidate miRNA}} - \text{Ct}_{\text{mi93 or U6}}$) as previously described (5). Fold change was calculated using the formula $2^{-\Delta\Delta\text{Ct}}$. miRNA levels were compared between groups using the KS test, a threshold of $P \leq 0.05$ was considered significant.

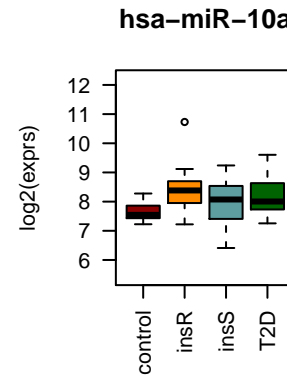
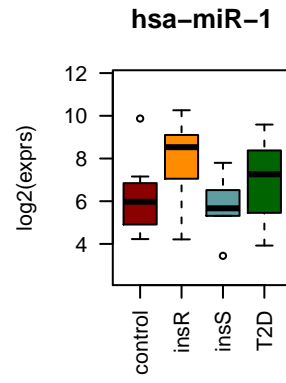
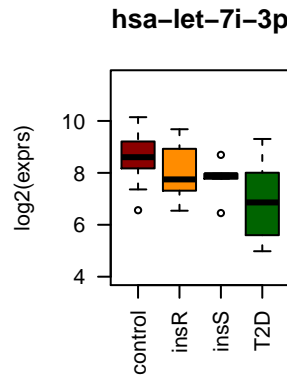
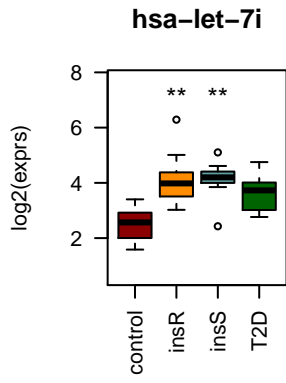
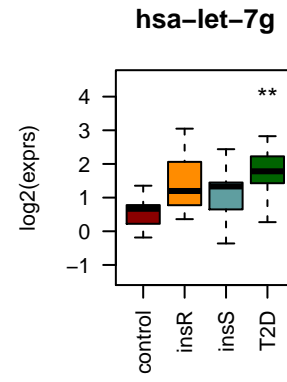
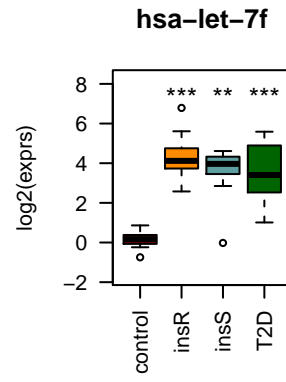
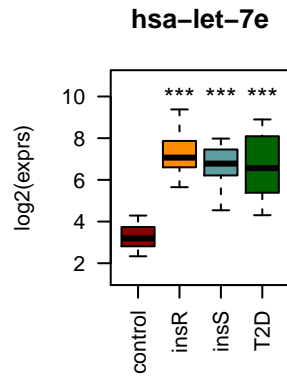
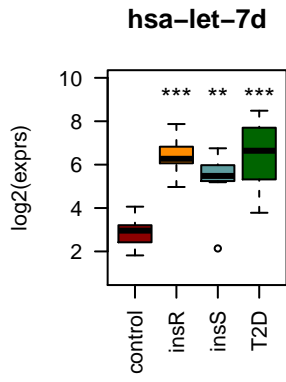
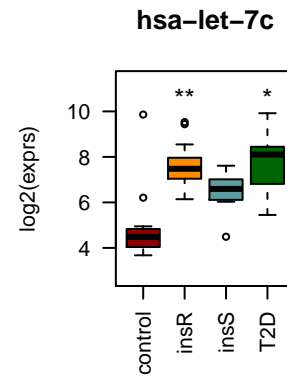
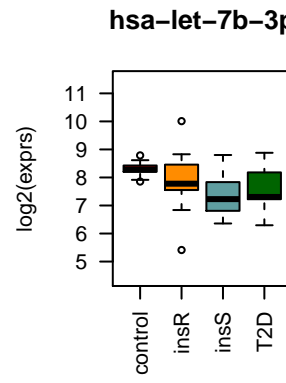
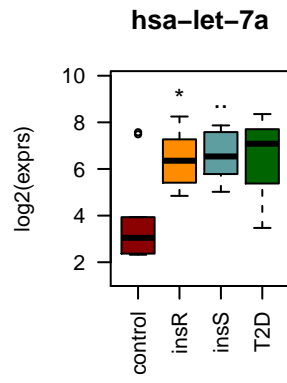
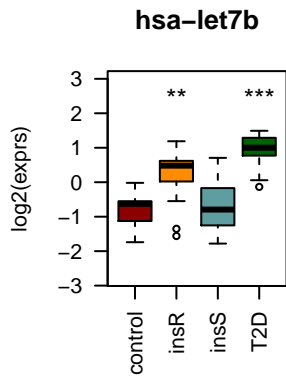
References:

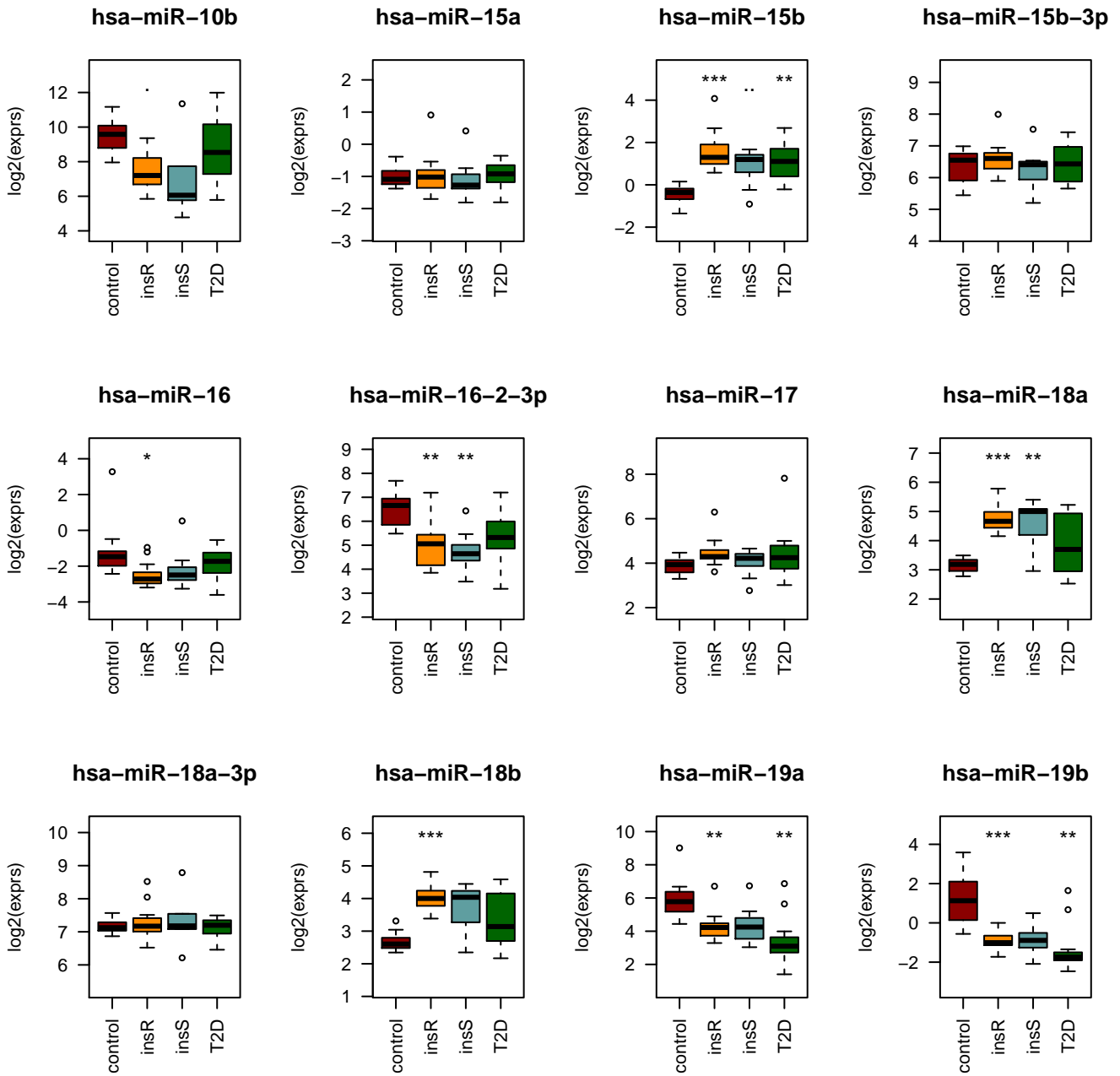
1. Enderle D, Spiel A, Coticchia CM, Berghoff E, Mueller R, Schlumpberger M, *et al.* Characterization of RNA from Exosomes and Other Extracellular Vesicles Isolated by a Novel Spin Column-Based Method. *Plos One* 2015;**10**.
2. R Core Team. *R: A language and environment for statistical computing*. R Foundation for Statistical Computing: Vienna, Austria, 2012.
3. Josse J, Husson F. missMDA: A Package for Handling Missing Values in Multivariate Data Analysis. *J Stat Softw* 2016;**70**.
4. Venables WN, Ripley BD. *Modern Applied Statistics with S*. Springer: New York, 2002.
5. Melman YF, Shah R, Danielson K, Xiao JJ, Simonson B, Barth A, *et al.* Circulating MicroRNA-30d Is Associated With Response to Cardiac Resynchronization Therapy in Heart Failure and Regulates Cardiomyocyte Apoptosis A Translational Pilot Study. *Circulation* 2015;**131**: 2202-2216.

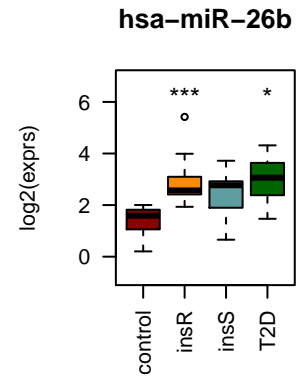
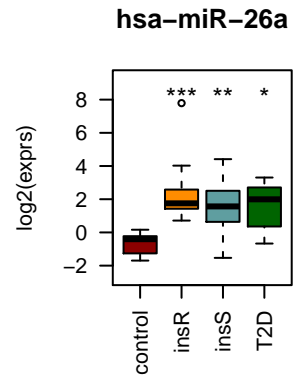
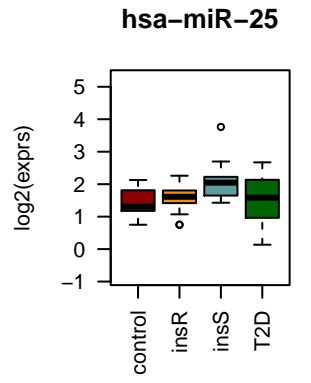
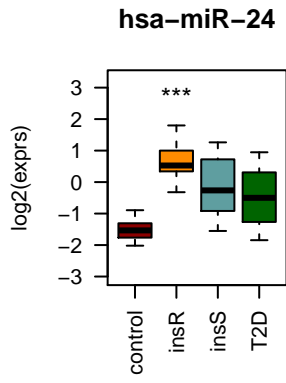
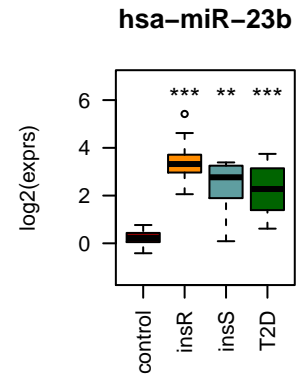
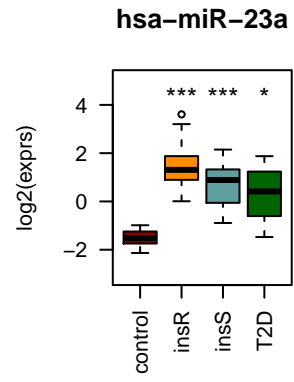
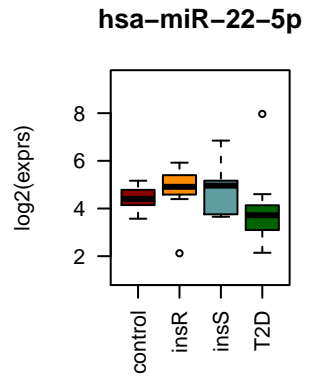
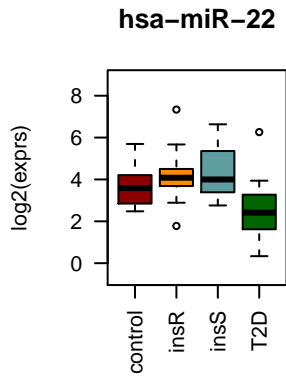
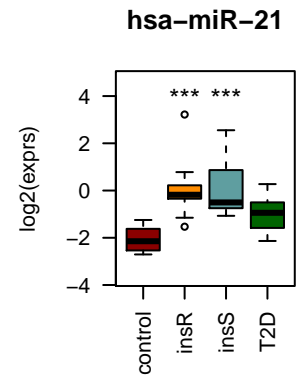
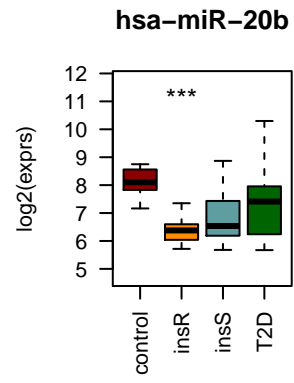
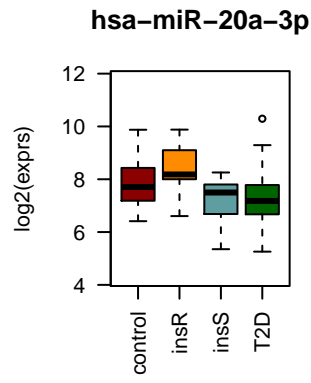
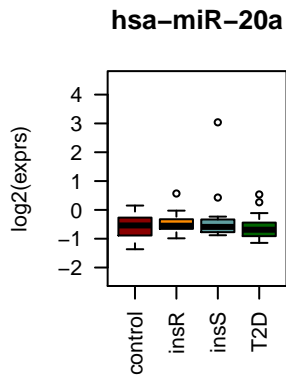
Supplementary File Figure S1

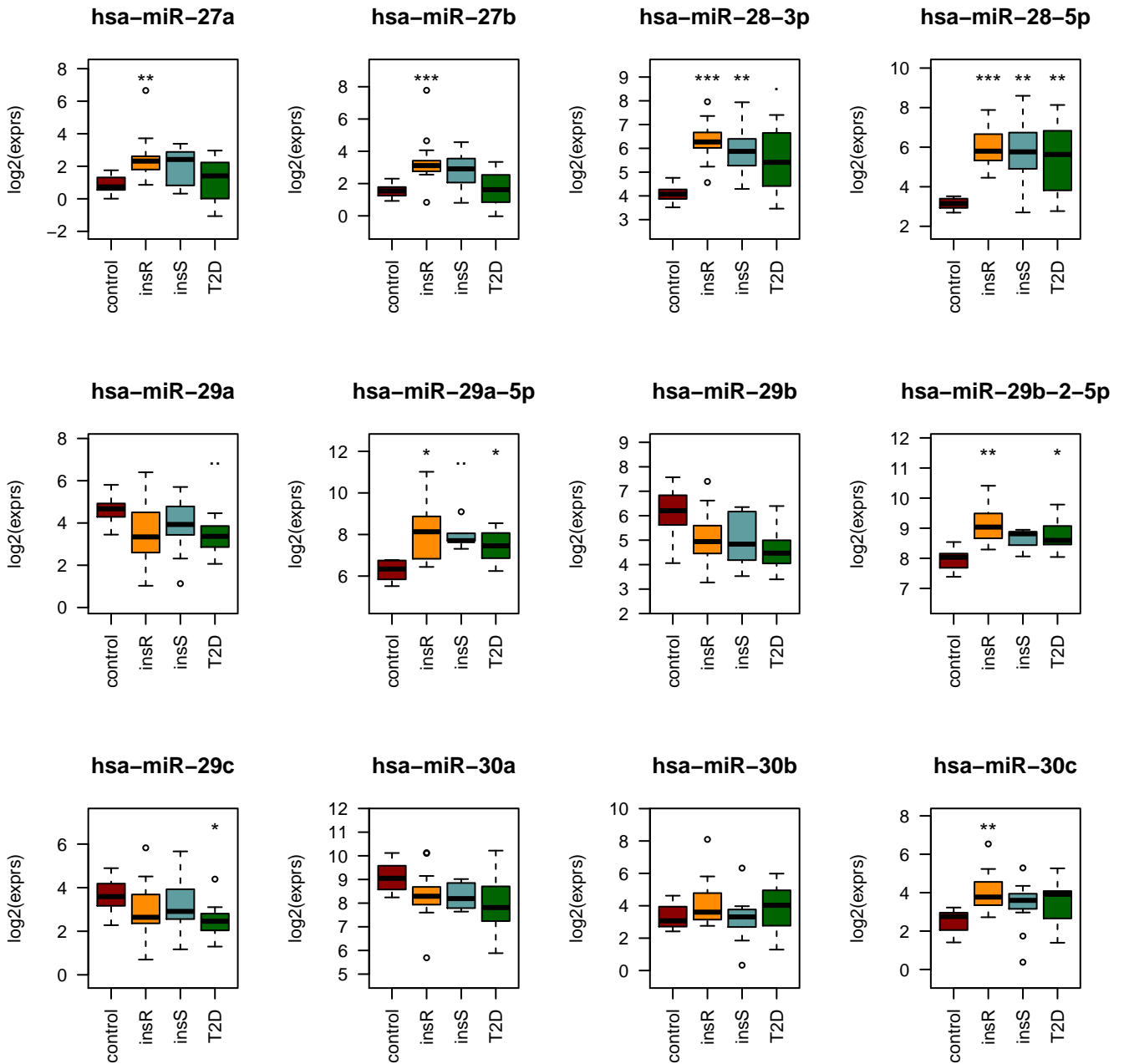
Boxplots showing log₂ expression (exprs) levels of circulating miRNA in plasma of control individuals without obesity, and individuals with three different obesity phenotypes - insulin sensitive, insulin resistance and type-two diabetes.

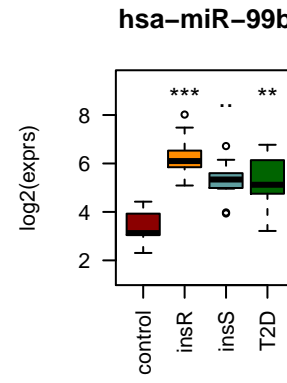
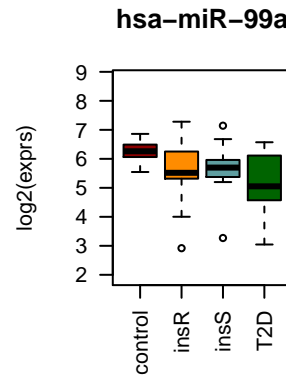
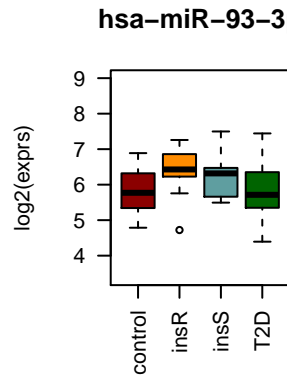
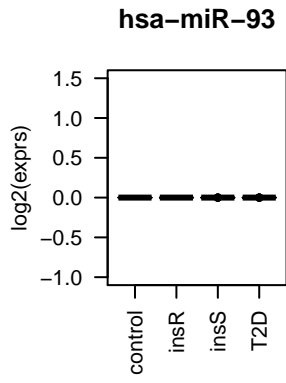
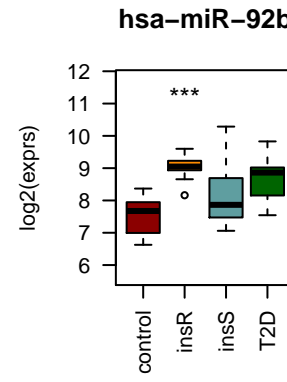
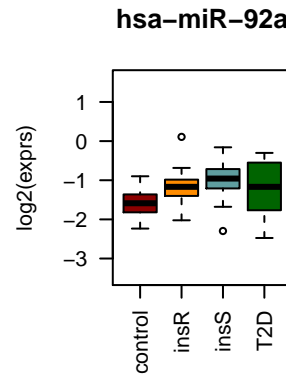
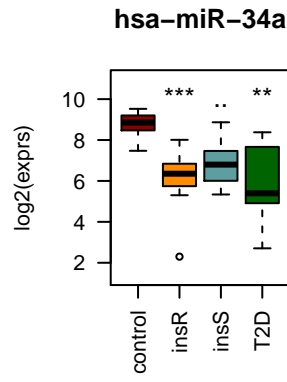
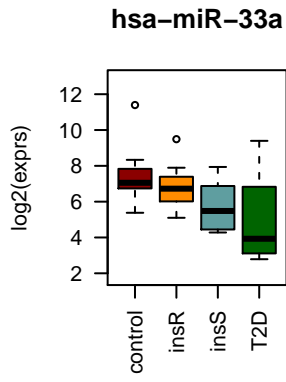
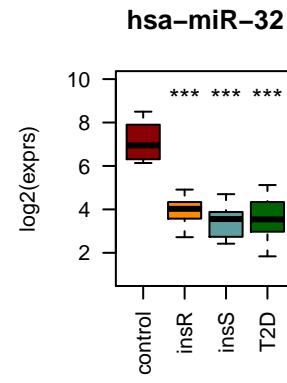
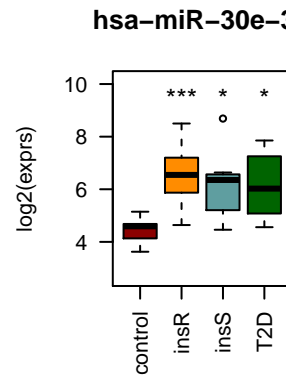
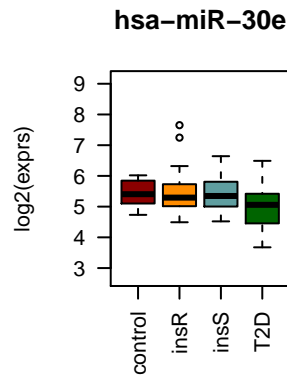
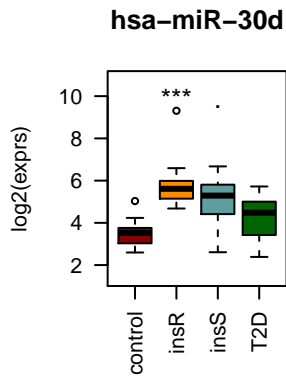
Log₂ expression (i.e. log₂ ΔCt) is shown on the Y axis. Significance levels are shown for comparisons between controls and each obese phenotypic group; they are presented as: Bonferroni adjusted P<0.05 *, <0.01 **, <0.001, *** and unadjusted P <0.01 and <0.001 are represented as a single or double dot respectively. Controls (red), inS (insulin sensitive, blue), insR (insulin resistant, yellow), T2D (type-II diabetes, green).

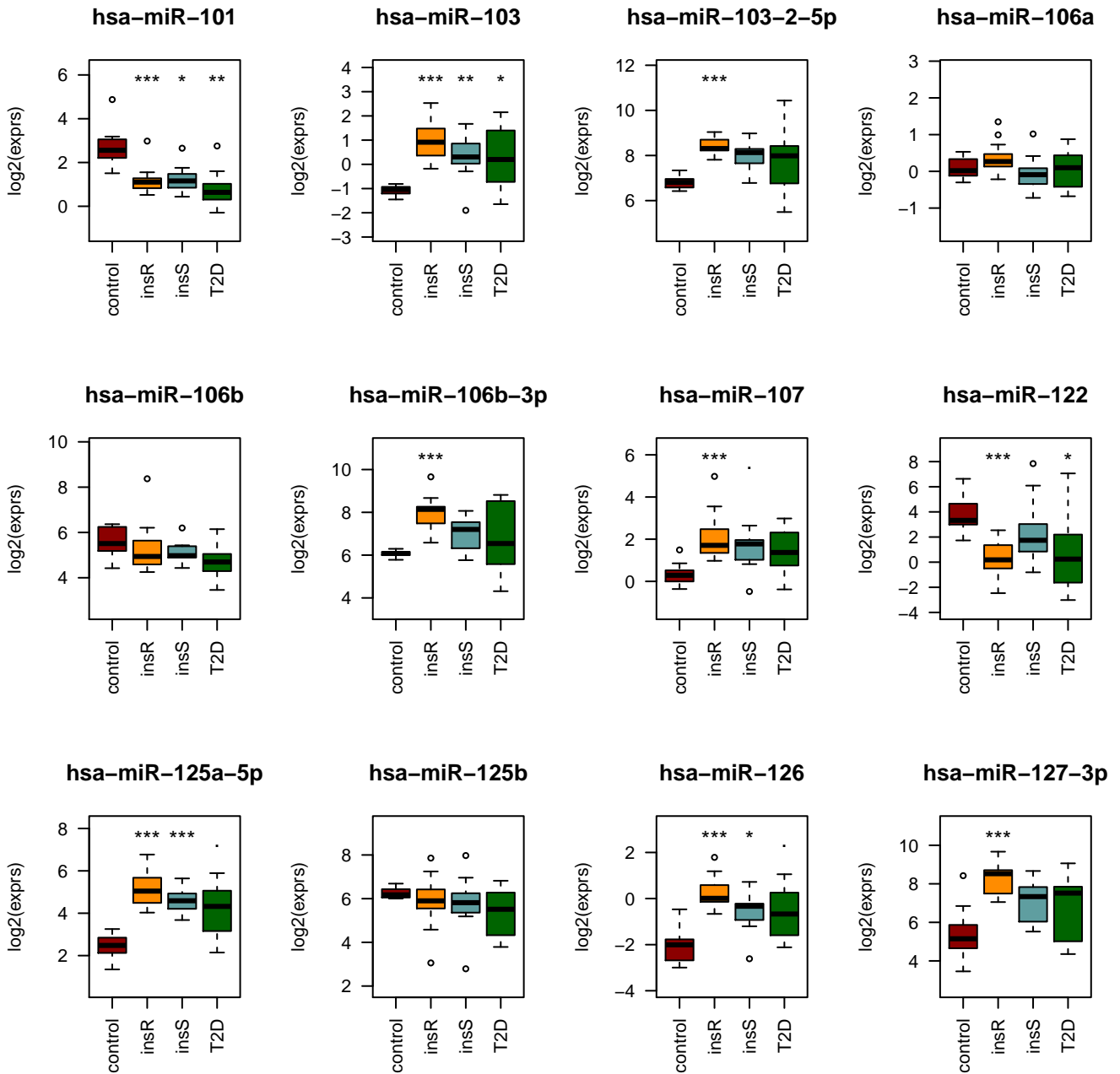


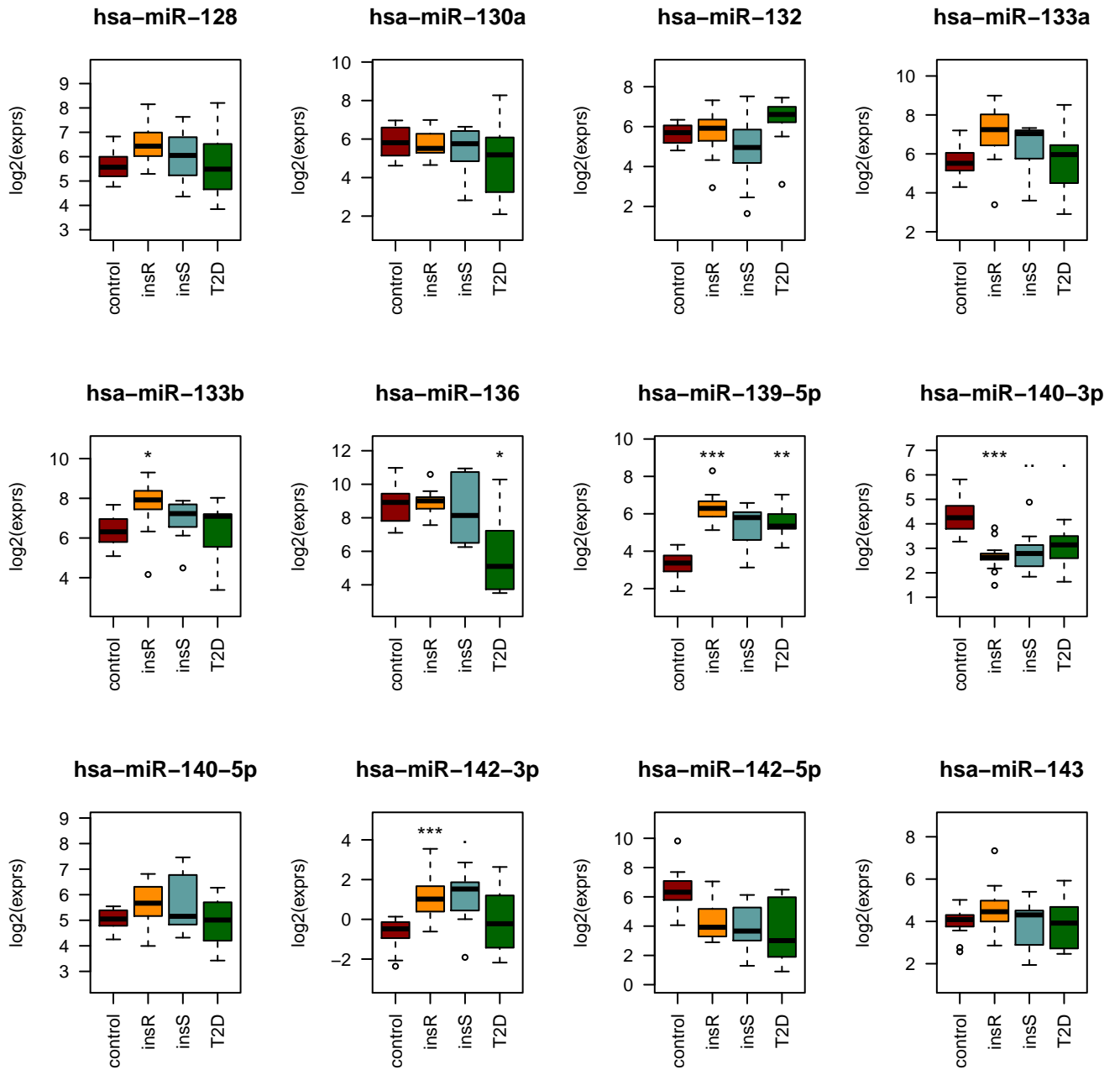


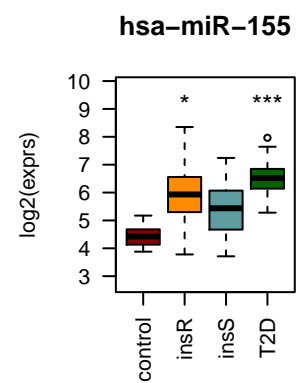
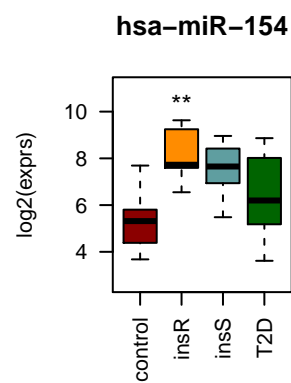
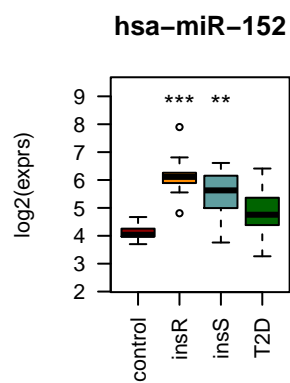
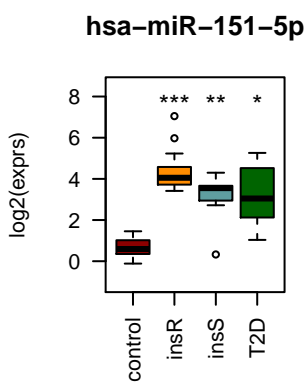
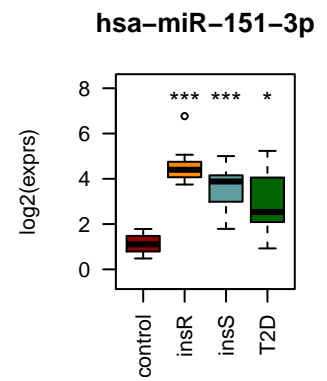
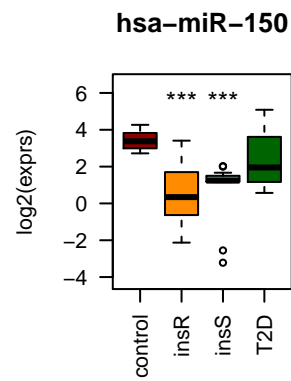
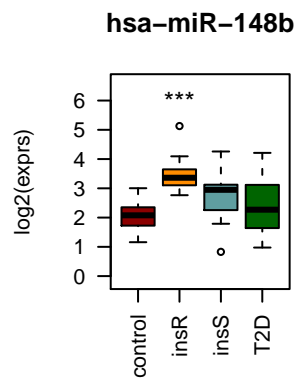
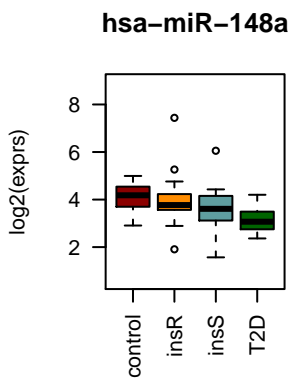
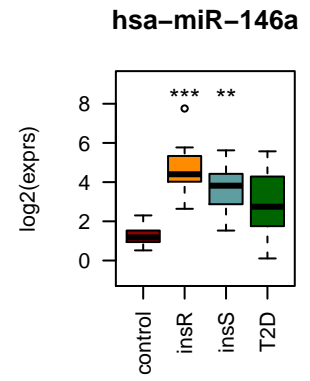
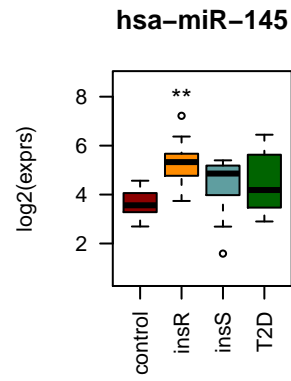
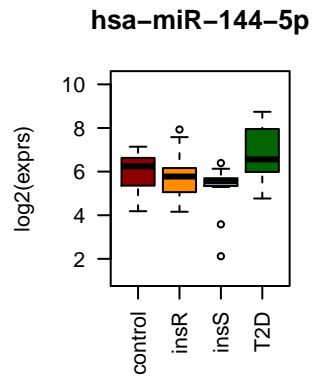
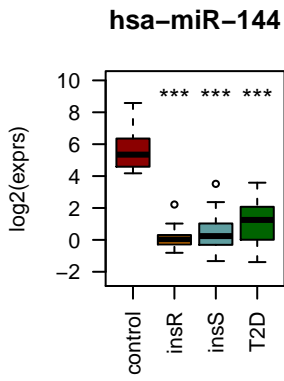


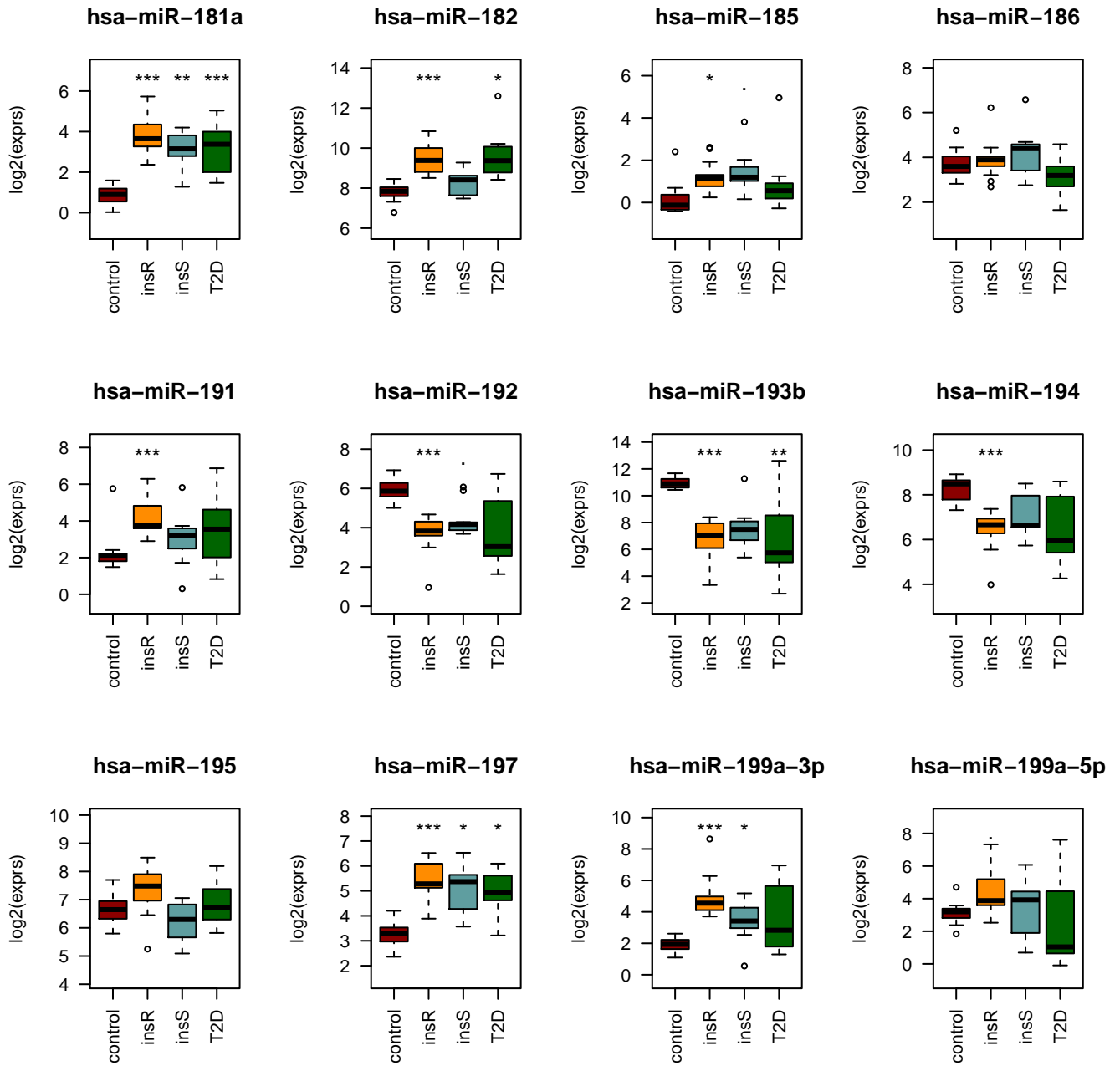


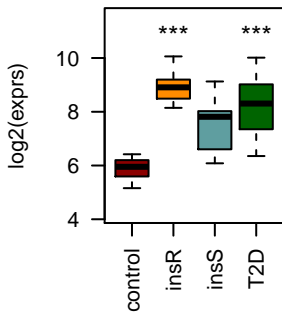
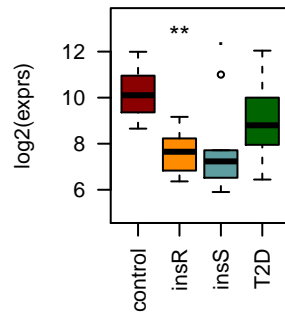
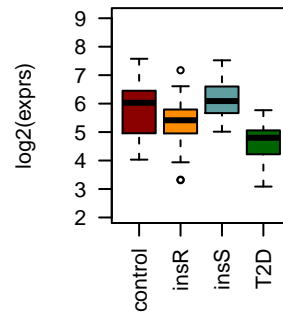
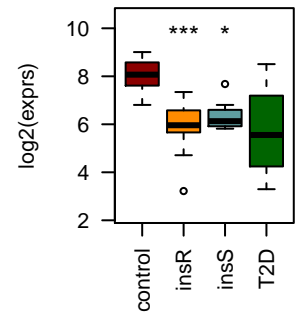
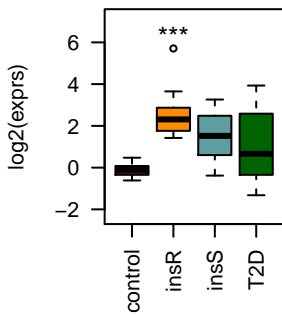
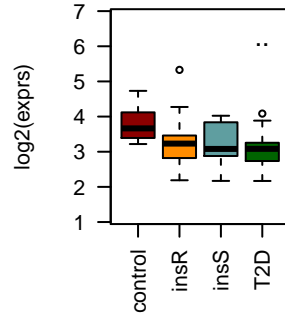
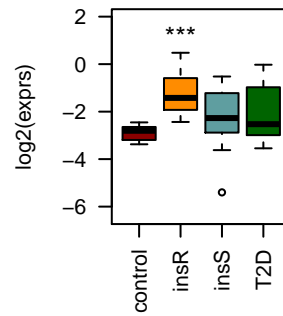
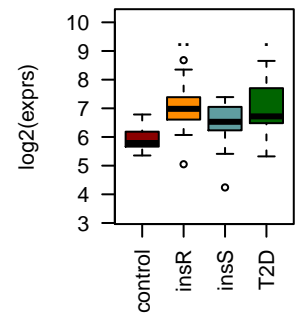
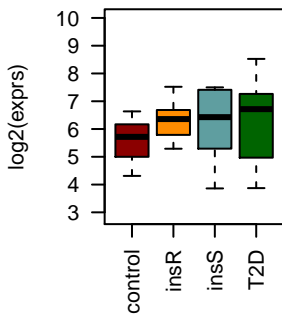
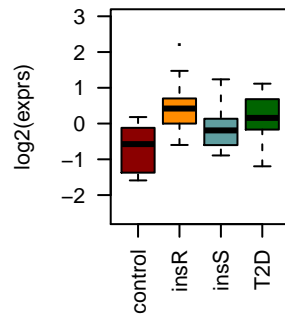
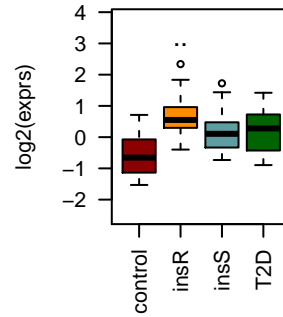
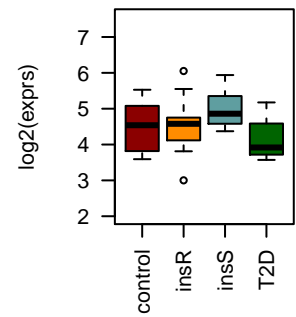


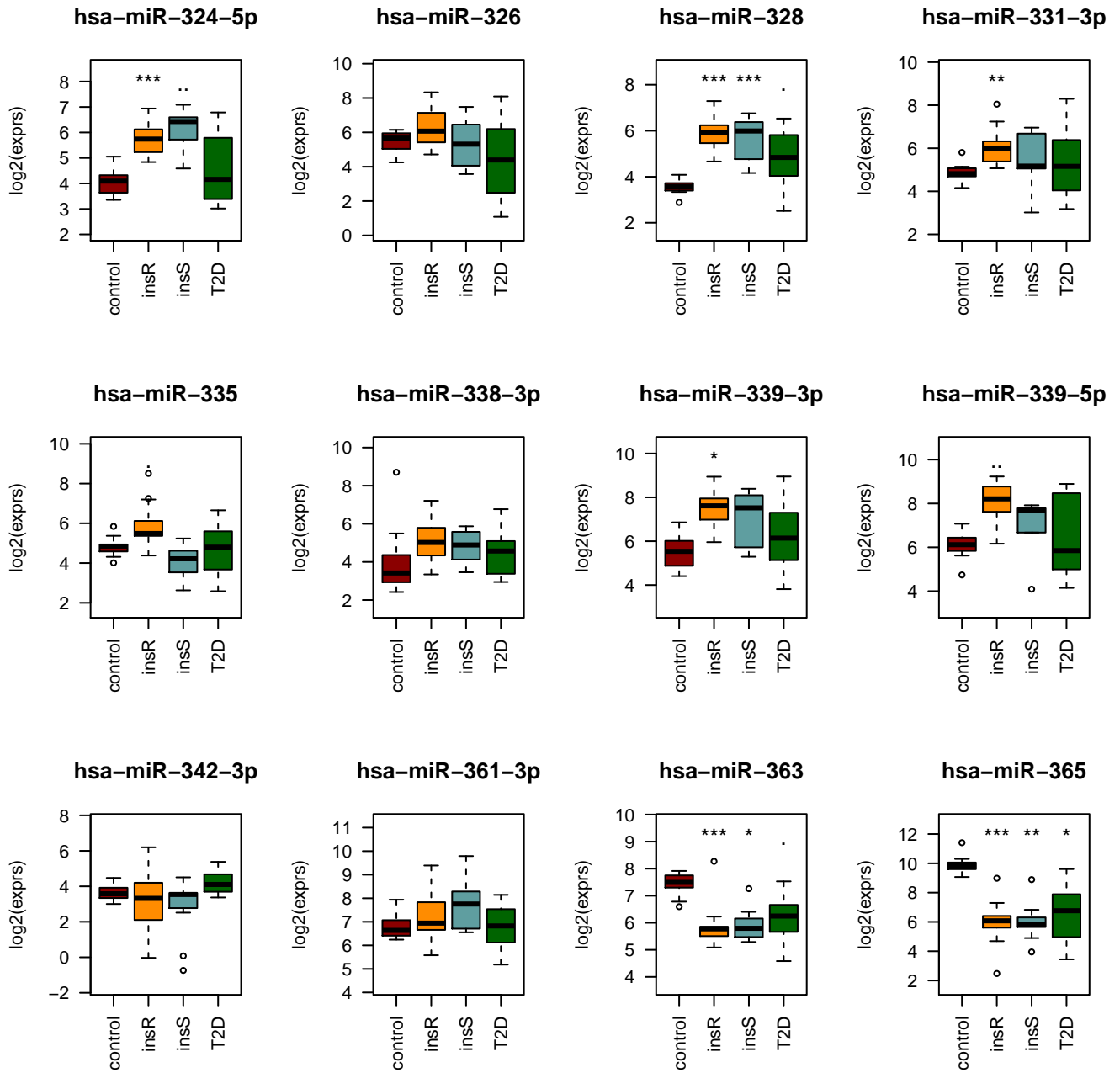


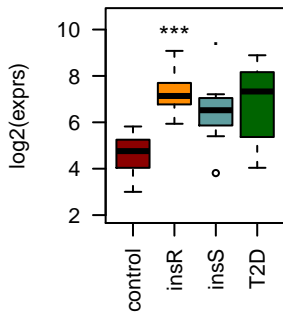
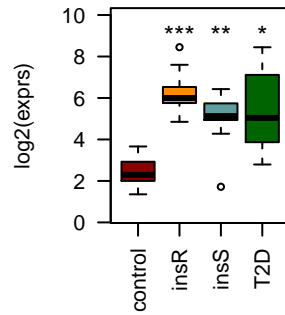
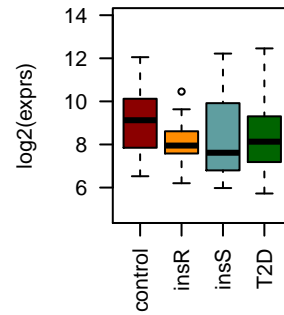
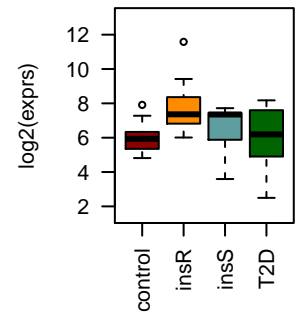
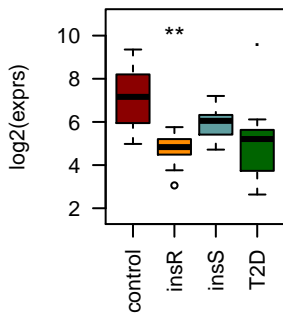
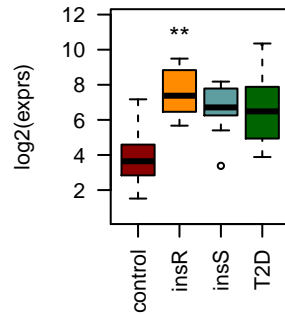
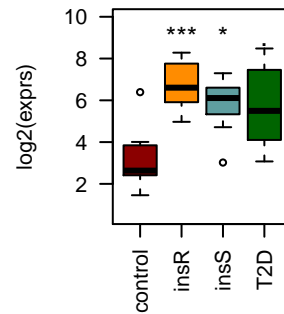
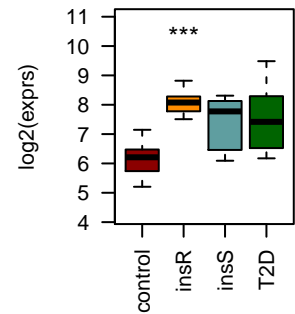
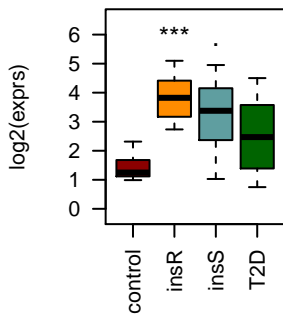
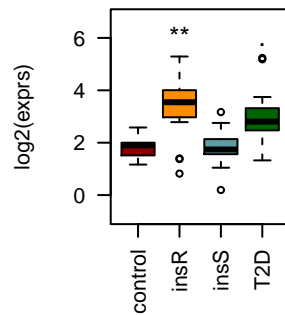
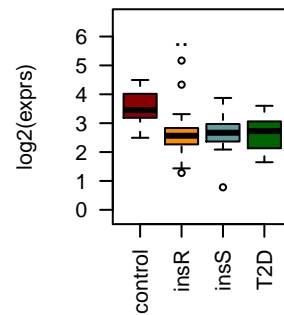
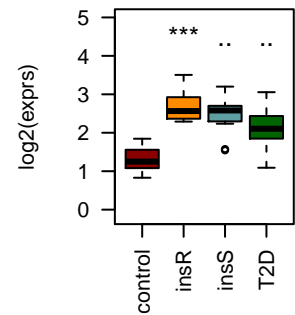


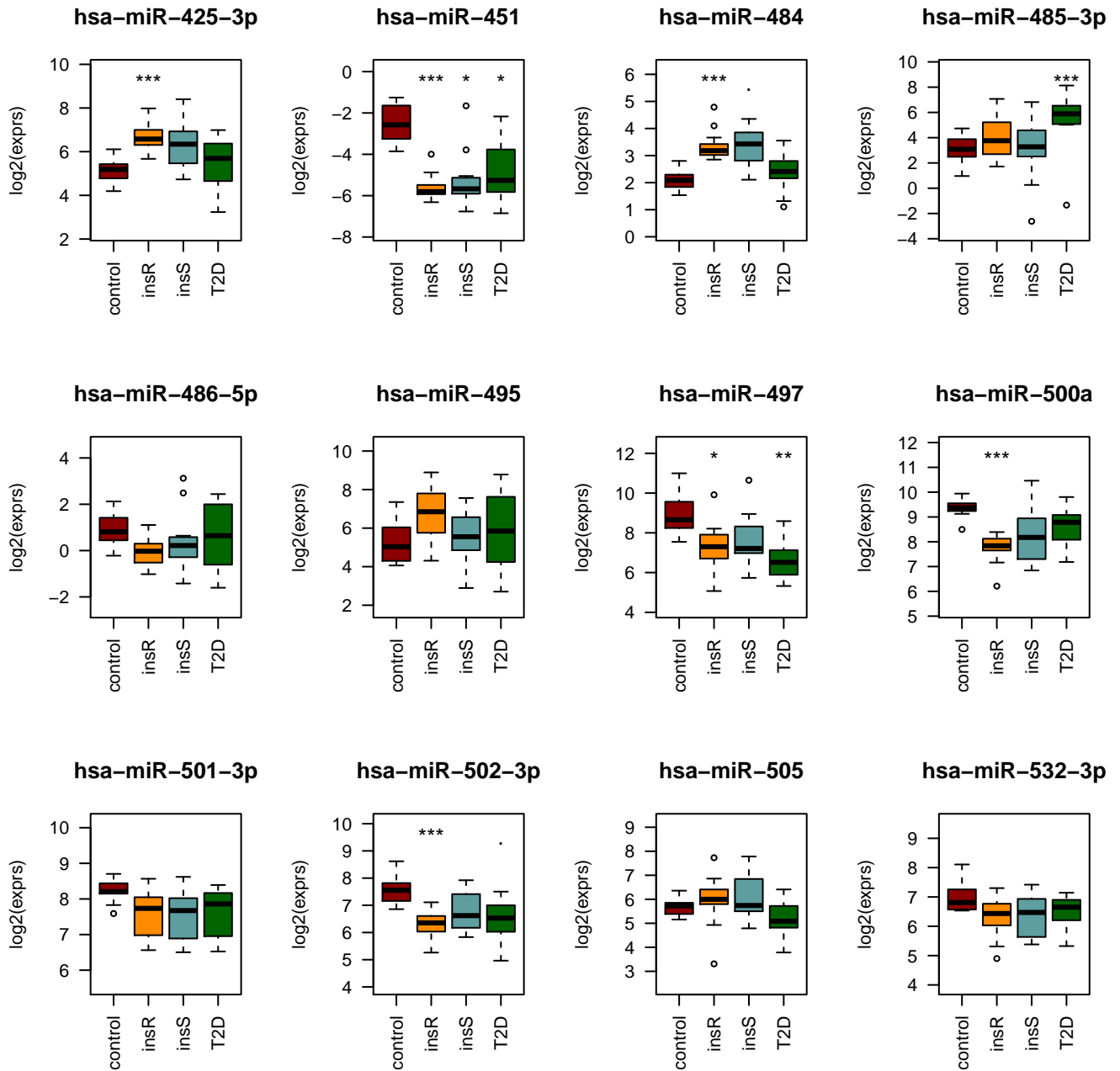


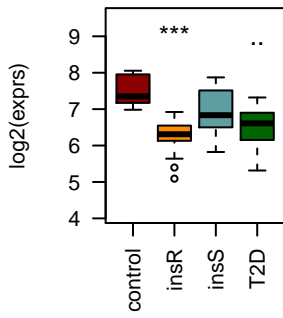
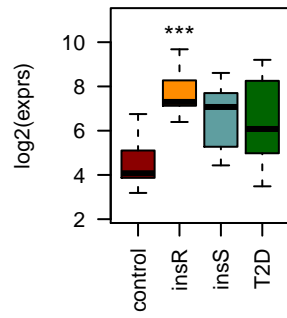
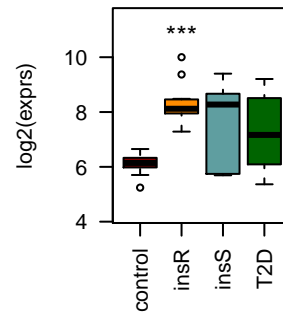
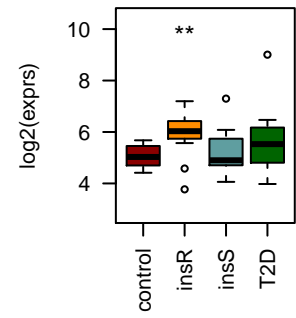
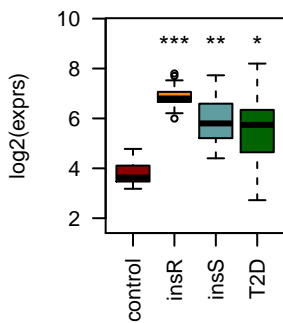
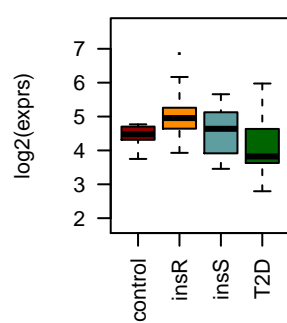
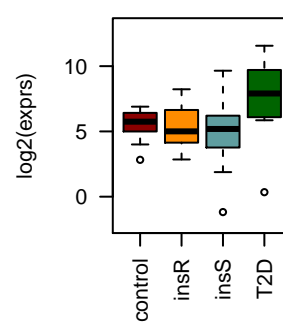
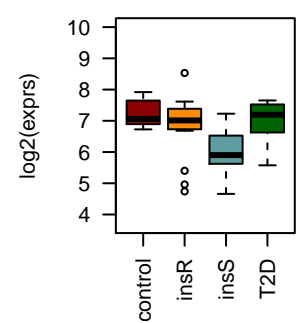
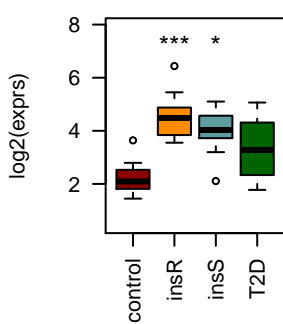
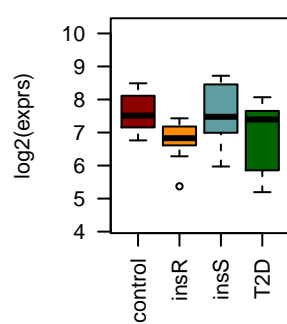
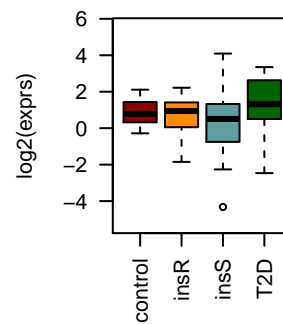
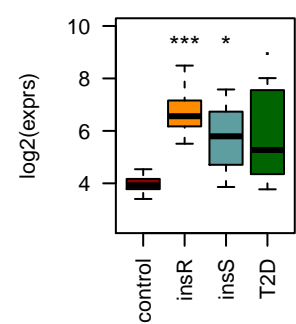


hsa-miR-200c**hsa-miR-205****hsa-miR-210****hsa-miR-215****hsa-miR-221****hsa-miR-222****hsa-miR-223****hsa-miR-223-5p****hsa-miR-301a****hsa-miR-320a****hsa-miR-320b****hsa-miR-324-3p**

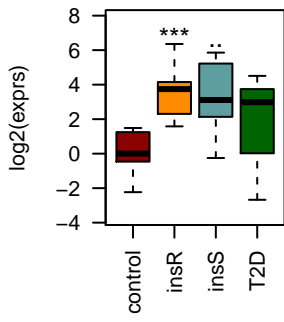


hsa-miR-374a**hsa-miR-374b****hsa-miR-375****hsa-miR-376a****hsa-miR-378****hsa-miR-382****hsa-miR-409-3p****hsa-miR-421****hsa-miR-423-3p****hsa-miR-423-5p****hsa-miR-424****hsa-miR-425**

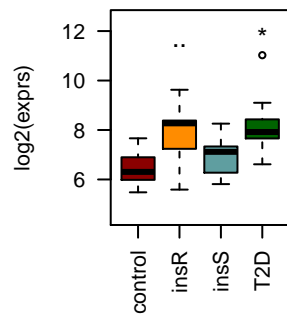


hsa-miR-532-5p**hsa-miR-543****hsa-miR-551b****hsa-miR-574-3p****hsa-miR-584****hsa-miR-590-5p****hsa-miR-605****hsa-miR-629****hsa-miR-652****hsa-miR-660****hsa-miR-720****hsa-miR-766**

hsa-miR-1974



hsa-miR-2110



Supplementary File Table S1:
Pearson's correlation data for all miRNA: clinical trait associations passing absolute $r \geq 0.3$ and adjusted $P \leq 0.05$.

Clinical Parameter	miRNA ⁺	Pearsons r	P value	Adjusted P value (fdr)
systolic blood pressure	hsa-let-7a	0.38	0.0102	0.0218
systolic blood pressure	hsa-let-7c	0.40	0.0059	0.0135
fasting-insulin	hsa-let-7d	0.47	0.0011	0.0029
HOMA2-IR	hsa-let-7d	0.41	0.0050	0.0117
McAuley-Index	hsa-let-7d	-0.43	0.0033	0.0081
systolic blood pressure	hsa-let-7d	0.36	0.0140	0.0288
fasting-glucose	hsa-let-7g	0.37	0.0121	0.0253
fasting-insulin	hsa-let-7g	0.33	0.0249	0.0477
HbA1c	hsa-let-7g	0.36	0.0163	0.0328
HOMA2-IR	hsa-let-7g	0.35	0.0199	0.0391
McAuley-Index	hsa-let-7g	-0.36	0.0152	0.0307
systolic blood pressure	hsa-let-7g	0.38	0.0091	0.0197
McAuley-Index	hsa-let-7b	-0.44	0.0024	0.0062
fasting-HDL	hsa-miR-122	0.34	0.0238	0.0458
fasting-insulin	hsa-miR-122	-0.46	0.0015	0.0041
fasting-triglycerides	hsa-miR-122	-0.41	0.0050	0.0116
HOMA2-IR	hsa-miR-122	-0.41	0.0057	0.0131
McAuley-Index	hsa-miR-122	0.56	0.0001	0.0003
fasting-triglycerides	hsa-miR-125b	-0.37	0.0112	0.0237
HbA1c	hsa-miR-136	-0.40	0.0068	0.0153
McAuley-Index	hsa-miR-144-5p	-0.36	0.0149	0.0303
diastolicBP	hsa-miR-145	0.39	0.0084	0.0184
HbA1c	hsa-miR-150	0.39	0.0090	0.0195
HbA1c	hsa-miR-152	-0.36	0.0146	0.0298
fasting-glucose	hsa-miR-155	0.33	0.0247	0.0474
HbA1c	hsa-miR-155	0.33	0.0260	0.0496
McAuley-Index	hsa-miR-155	-0.34	0.0236	0.0455
systolic blood pressure	hsa-miR-155	0.41	0.0050	0.0117
fasting-insulin	hsa-miR-15b	0.34	0.0234	0.0451
fasting-LDL	hsa-miR-17	-0.34	0.0206	0.0404
systolic blood pressure	hsa-miR-17	0.36	0.0147	0.0300
systolic blood pressure	hsa-miR-181a	0.33	0.0253	0.0484
fasting-insulin	hsa-miR-192	-0.41	0.0046	0.0108
fasting-triglycerides	hsa-miR-192	-0.40	0.0071	0.0159
HOMA2-IR	hsa-miR-192	-0.38	0.0093	0.0202
McAuley-Index	hsa-miR-192	0.38	0.0111	0.0235
systolic blood pressure	hsa-miR-192	-0.33	0.0261	0.0497
fasting-HDL	hsa-miR-193b	0.34	0.0213	0.0416
fasting-insulin	hsa-miR-193b	-0.35	0.0175	0.0348
fasting-triglycerides	hsa-miR-193b	-0.46	0.0015	0.0041

HOMA2-IR	hsa-miR-193b	-0.36	0.0153	0.0310
McAuley-Index	hsa-miR-193b	0.38	0.0096	0.0207
systolic blood pressure	hsa-miR-193b	-0.36	0.0152	0.0307
fasting-triglycerides	hsa-miR-194	-0.41	0.0048	0.0113
systolic blood pressure	hsa-miR-199a-3p	0.34	0.0225	0.0436
fasting-triglycerides	hsa-miR-21	-0.43	0.0029	0.0073
fasting-glucose	hsa-miR-210	-0.42	0.0044	0.0104
fasting-HDL	hsa-miR-210	0.37	0.0122	0.0255
fasting-insulin	hsa-miR-210	-0.40	0.0071	0.0159
fasting-triglycerides	hsa-miR-210	-0.41	0.0050	0.0116
HbA1c	hsa-miR-210	-0.43	0.0036	0.0086
HOMA2-IR	hsa-miR-210	-0.36	0.0141	0.0290
McAuley-Index	hsa-miR-210	0.48	0.0009	0.0025
McAuley-Index	hsa-miR-2110	-0.37	0.0126	0.0262
fasting-insulin	hsa-miR-215	-0.40	0.0067	0.0152
fasting-triglycerides	hsa-miR-215	-0.44	0.0027	0.0069
HOMA2-IR	hsa-miR-215	-0.37	0.0115	0.0243
McAuley-Index	hsa-miR-215	0.37	0.0118	0.0247
fasting-glucose	hsa-miR-22	-0.41	0.0047	0.0110
fasting-HDL	hsa-miR-22	0.35	0.0179	0.0357
fasting-triglycerides	hsa-miR-22	-0.43	0.0030	0.0075
HbA1c	hsa-miR-22	-0.42	0.0036	0.0088
fasting-triglycerides	hsa-miR-22-5p	-0.42	0.0043	0.0103
fasting-insulin	hsa-miR-223-5p	0.39	0.0085	0.0185
McAuley-Index	hsa-miR-223-5p	-0.34	0.0206	0.0403
fasting-insulin	hsa-miR-25	-0.45	0.0019	0.0049
HOMA2-IR	hsa-miR-25	-0.39	0.0074	0.0164
McAuley-Index	hsa-miR-25	0.33	0.0246	0.0473
systolic blood pressure	hsa-miR-26b	0.38	0.0109	0.0232
fasting-triglycerides	hsa-miR-27b	-0.38	0.0109	0.0232
HbA1c	hsa-miR-27b	-0.33	0.0257	0.0490
fasting-triglycerides	hsa-miR-30a	-0.41	0.0057	0.0130
fasting-insulin	hsa-miR-30b	0.34	0.0224	0.0434
fasting-insulin	hsa-miR-30e-3p	0.34	0.0232	0.0449
fasting-insulin	hsa-miR-335	0.39	0.0076	0.0168
fasting-HDL	hsa-miR-34a	0.39	0.0076	0.0168
fasting-insulin	hsa-miR-34a	-0.45	0.0022	0.0055
fasting-triglycerides	hsa-miR-34a	-0.49	0.0006	0.0017
HOMA2-IR	hsa-miR-34a	-0.43	0.0031	0.0075
McAuley-Index	hsa-miR-34a	0.49	0.0006	0.0017
fasting-insulin	hsa-miR-374a	0.36	0.0152	0.0309
HOMA2-IR	hsa-miR-374a	0.34	0.0212	0.0414
fasting-insulin	hsa-miR-374b	0.37	0.0112	0.0237
fasting-glucose	hsa-miR-378	-0.36	0.0167	0.0335

fasting-HDL	hsa-miR-378	0.49	0.0006	0.0017
fasting-insulin	hsa-miR-378	-0.54	0.0001	0.0004
fasting-triglycerides	hsa-miR-378	-0.47	0.0012	0.0032
HOMA2-IR	hsa-miR-378	-0.52	0.0003	0.0008
McAuley-Index	hsa-miR-378	0.51	0.0003	0.0011
fasting-insulin	hsa-miR-421	0.39	0.0075	0.0166
McAuley-Index	hsa-miR-423-5p	-0.33	0.0258	0.0492
fasting-glucose	hsa-miR-484	-0.35	0.0171	0.0342
fasting-triglycerides	hsa-miR-484	-0.35	0.0194	0.0382
HbA1c	hsa-miR-484	-0.39	0.0082	0.0180
fasting-insulin	hsa-miR-495	0.36	0.0138	0.0284
HOMA2-IR	hsa-miR-495	0.35	0.0177	0.0352
fasting-triglycerides	hsa-miR-502-3p	-0.33	0.0259	0.0495
fasting-HDL	hsa-miR-505	0.35	0.0185	0.0366
fasting-triglycerides	hsa-miR-505	-0.50	0.0005	0.0014
HbA1c	hsa-miR-505	-0.36	0.0165	0.0332
fasting-triglycerides	hsa-miR-532-5p	-0.44	0.0026	0.0066
McAuley-Index	hsa-miR-532-5p	0.42	0.0039	0.0093
fasting-triglycerides	hsa-miR-660	-0.45	0.0018	0.0047
McAuley-Index	hsa-miR-660	0.39	0.0077	0.0170
fasting-insulin	hsa-miR-766	0.34	0.0213	0.0416
fasting-triglycerides	hsa-miR-99a	-0.45	0.0020	0.0052
McAuley-Index	hsa-miR-99a	0.34	0.0241	0.0463

Supplementary References in Tables 2 and 3

- S1. Ferrante SC, Nadler EP, Pillai DK, Hubal MJ, Wang ZY, Wang JM, *et al.* Adipocyte-derived exosomal miRNAs: a novel mechanism for obesity-related disease. *Pediatric research* 2015;**77**: 447-454.
- S2. Karbiener M, Pisani DF, Frontini A, Oberreiter LM, Lang E, Vegiopoulos A, *et al.* MicroRNA-26 Family Is Required for Human Adipogenesis and Drives Characteristics of Brown Adipocytes. *Stem Cells* 2014;**32**: 1578-1590.
- S3. Fu XH, Dong BN, Tian Y, Lefebvre P, Meng ZP, Wang XC, *et al.* MicroRNA-26a regulates insulin sensitivity and metabolism of glucose and lipids. *Journal of Clinical Investigation* 2015;**125**: 2497-2509.
- S4. Chartoumpakis DV, Zaravinos A, Ziros PG, Iskrenova RP, Psyrogiannis AI, Kyriazopoulou VE, *et al.* Differential Expression of MicroRNAs in Adipose Tissue after Long-Term High-Fat Diet-Induced Obesity in Mice. *Plos One* 2012;**7**.
- S5. Arner E, Mejhert N, Kulyte A, Balwiercz PJ, Pachkov M, Cormont M, *et al.* Adipose tissue microRNAs as regulators of CCL2 production in human obesity. *Diabetes* 2012;**61**: 1986-1993.
- S6. Zhou B, Li C, Qi W, Zhang Y, Zhang F, Wu JX, *et al.* Downregulation of miR-181a upregulates sirtuin-1 (SIRT1) and improves hepatic insulin sensitivity. *Diabetologia* 2012;**55**: 2032-2043.
- S7. Hulsmans M, Sinnaeve P, Van der Schueren B, Mathieu C, Janssens S, Holvoet P. Decreased miR-181a Expression in Monocytes of Obese Patients Is Associated with the Occurrence of Metabolic Syndrome and Coronary Artery Disease. *Journal of Clinical Endocrinology & Metabolism* 2012;**97**: E1213-E1218.
- S8. Chu B, Wu T, Miao L, Mei YD, Wu MA. MiR-181a regulates lipid metabolism via IDH1. *Scientific reports* 2015;**5**.
- S9. Flowers E, Gadgil M, Aouizerat BE, Kanaya AM. Circulating micrnas associated with glycemic impairment and progression in Asian Indians. *Biomarker Research* 2015;**3**.
- S10. Santovito D, De Nardis V, Marcantonio P, Mandolini C, Paganelli C, Vitale E, *et al.* Plasma Exosome MicroRNA Profiling Unravels a New Potential Modulator of Adiponectin Pathway in Diabetes: Effect of Glycemic Control. *Journal of Clinical Endocrinology & Metabolism* 2014;**99**: E1681-E1685.
- S11. Karolina DS, Armugam A, Tavintharan S, Wong MTK, Lim SC, Sum CF, *et al.* MicroRNA 144 Impairs Insulin Signaling by Inhibiting the Expression of Insulin Receptor Substrate 1 in Type 2 Diabetes Mellitus. *Plos One* 2011;**6**.
- S12. Vega-Badillo J, Gutierrez-Vidal R, Hernandez-Perez HA, Villamil-Ramirez H, Leon-Mimila P, Sanchez-Munoz F, *et al.* Hepatic miR-33a/miR-144 and their target gene ABCA1 are associated with steatohepatitis in morbidly obese subjects. *Liver international : official journal of the International Association for the Study of the Liver* 2016.

- S13. Sun L, Xie H, Mori MA, Alexander R, Yuan B, Hattangadi SM, *et al.* Mir193b-365 is essential for brown fat differentiation. *Nature cell biology* 2011;**13**: 958-965.
- S14. Mori MA, Thomou T, Boucher J, Lee KY, Lallukka S, Kim JK, *et al.* Altered miRNA processing disrupts brown/white adipocyte determination and associates with lipodystrophy. *J Clin Invest* 2014;**124**: 3339-3351.
- S15. Kuang LR, Sewe M, Wang Y. A Pilot Study: The Effect of Roux-en-Y Gastric Bypass on the Serum MicroRNAs of the Type 2 Diabetes Patient. *Obesity Surgery* 2015;**25**: 2386-2392.
- S16. Kuwabara Y, Horie T, Baba O, Watanabe S, Nishiga M, Usami S, *et al.* MicroRNA-451 Exacerbates Lipotoxicity in Cardiac Myocytes and High-Fat Diet-Induced Cardiac Hypertrophy in Mice Through Suppression of the LKB1/AMPK Pathway. *Circulation research* 2015;**116**: 279-U217.
- S17. Ying W, Tseng A, Chang RCA, Wang HQ, Lin YL, Kanameni S, *et al.* miR-150 regulates obesity-associated insulin resistance by controlling B cell functions. *Scientific reports* 2016;**6**.
- S18. Zeng LQ, Wei SB, Sun YM, Qin WY, Cheng J, Mitchelson K, *et al.* Systematic profiling of mRNA and miRNA expression in the pancreatic islets of spontaneously diabetic Goto-Kakizaki rats. *Molecular Medicine Reports* 2015;**11**: 67-74.
- S19. Belarbi Y, Mejhert N, Lorente-Cebrian S, Dahlman I, Arner P, Ryden M, *et al.* MicroRNA-193b Controls Adiponectin Production in Human White Adipose Tissue. *Journal of Clinical Endocrinology & Metabolism* 2015;**100**: E1084-E1088.
- S20. Wu Q, Li JV, Seyfried F, le Roux CW, Ashrafian H, Athanasiou T, *et al.* Metabolic phenotype-microRNA data fusion analysis of the systemic consequences of Roux-en-Y gastric bypass surgery. *International Journal of Obesity (Lond)* 2015; **39**: 1126-1134.
- S21. Fu TM, Choi SG, Huang Z, Suino-Powell K, Xu HE, Kemper B, *et al.* MicroRNA 34a Inhibits Beige and Brown Fat Formation in Obesity in Part by Suppressing Adipocyte Fibroblast Growth Factor 21 Signaling and SIRT1 Function. *Molecular and cellular biology* 2014;**34**: 4130-4142.
- S22. Choi SE, Fu T, Seok S, Kim DH, Yu E, Lee KW, *et al.* Elevated microRNA-34a in obesity reduces NAD(+) levels and SIRT1 activity by directly targeting NAMPT. *Aging Cell* 2013;**12**: 1062-1072.
- S23. Fu T, Choi SE, Kim DH, Seok S, Suino-Powell KM, Xu HE, *et al.* Aberrantly elevated microRNA-34a in obesity attenuates hepatic responses to FGF19 by targeting a membrane coreceptor beta-Klotho. *Proceedings of the National Academy of Sciences of the United States of America* 2012;**109**: 16137-16142.