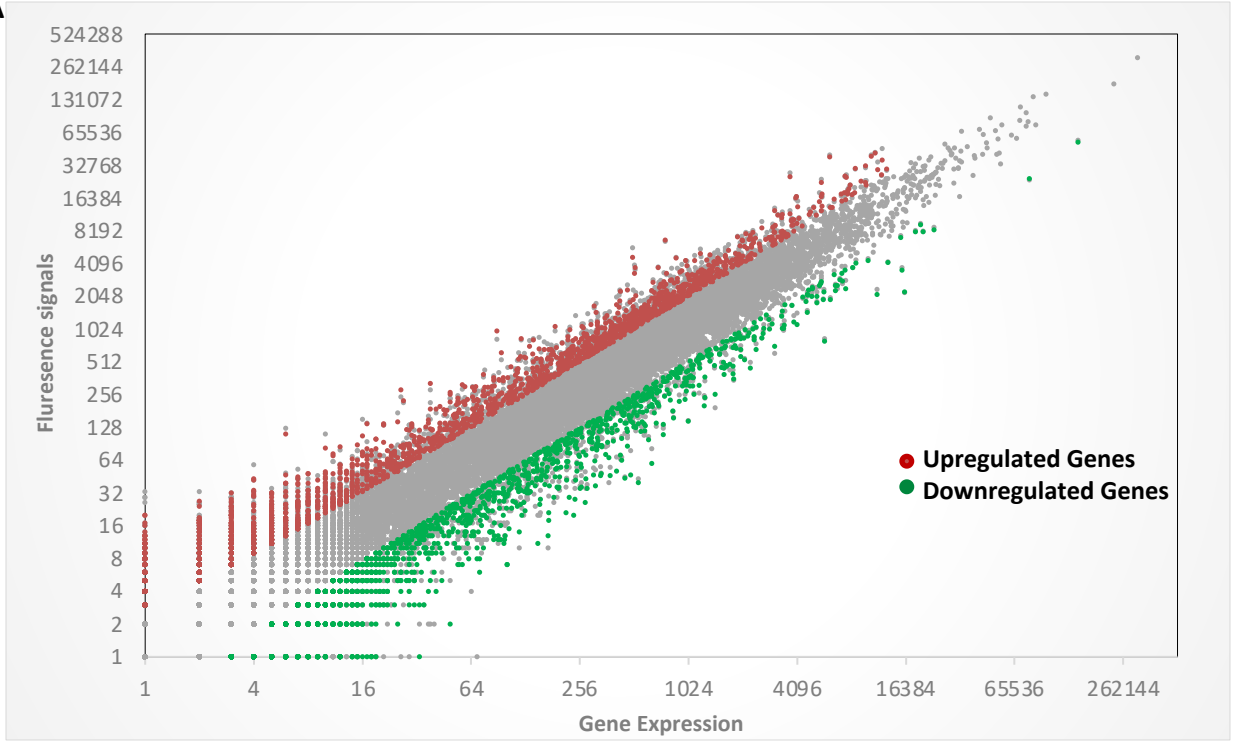
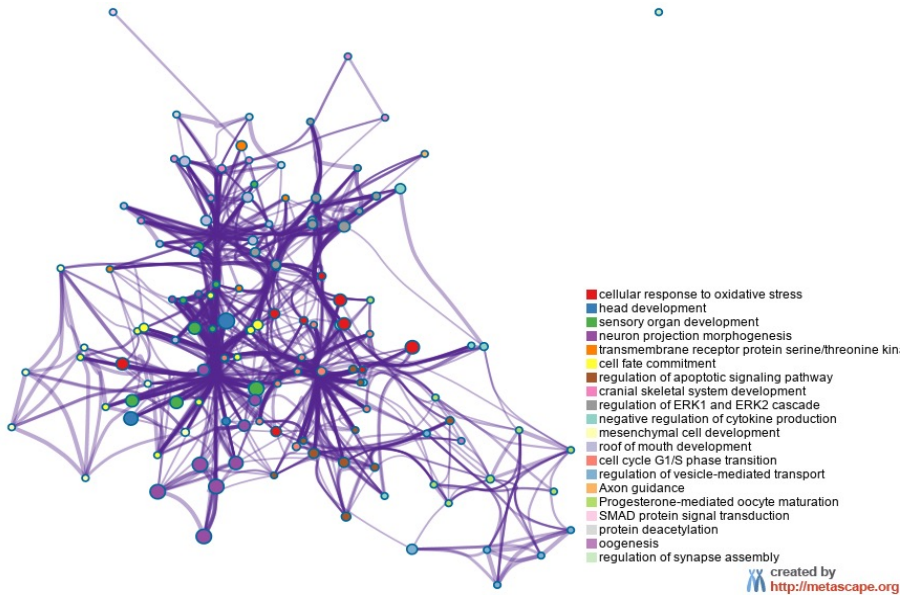
A



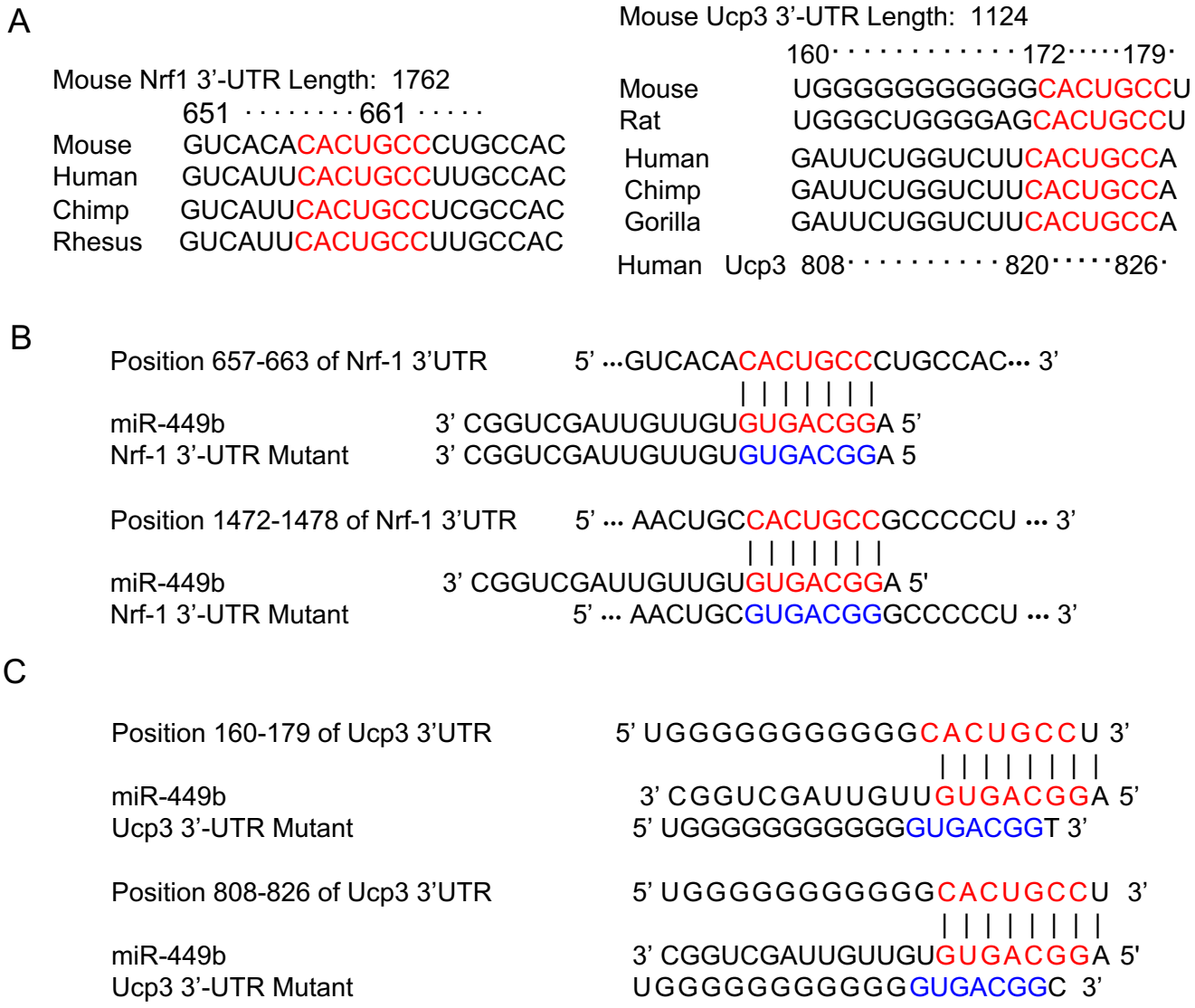
B



A. GSE77251 Pubmed database was analyzed. Dots represented regulated genes in human primary cells responsive to miR-449b. Red, upregulation; Green, downregulation. Grey, no changes.

B. Metascape online Go analysis on the biological pathways regulated by these 72 genes.

Supplemental Figure 1

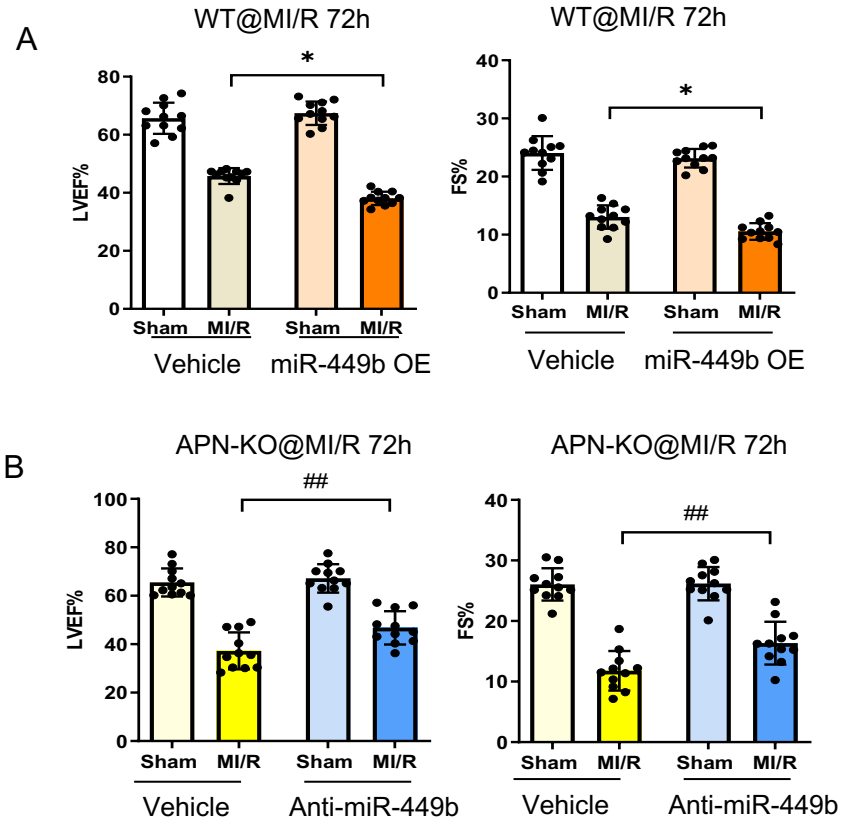


Supplemental Figure 2

A. Schematic representation of miRNA 449b sequence preservation, especially of the seed sequence in mammals.

B. Genomic localization and organization of miRNA 449b and Nrf-1 in mice. Schematic diagram representing the site-directed mutagenesis performed in 3'UTR of mice Nrf-1. Schematic diagram representing the site-directed mutagenesis performed in 3'UTR of mice Nrf-1.

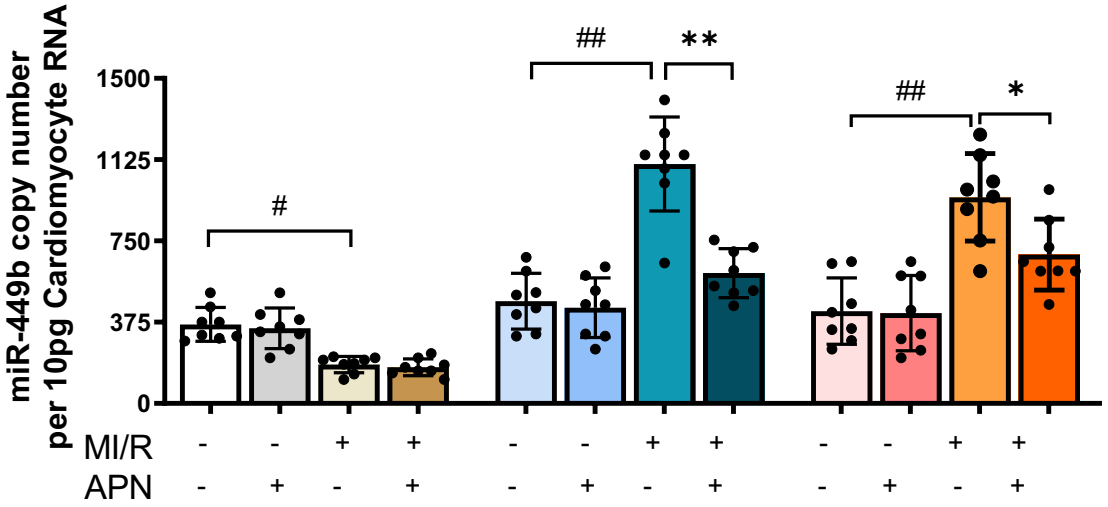
C. Genomic localization and organization of miRNA 449b and Ucp3 in mice. Schematic diagram representing the site-directed mutagenesis performed in 3'UTR of mice Ucp3. Schematic diagram representing the site-directed mutagenesis performed in 3'UTR of mice Ucp3 .



Supplemental Figure 3

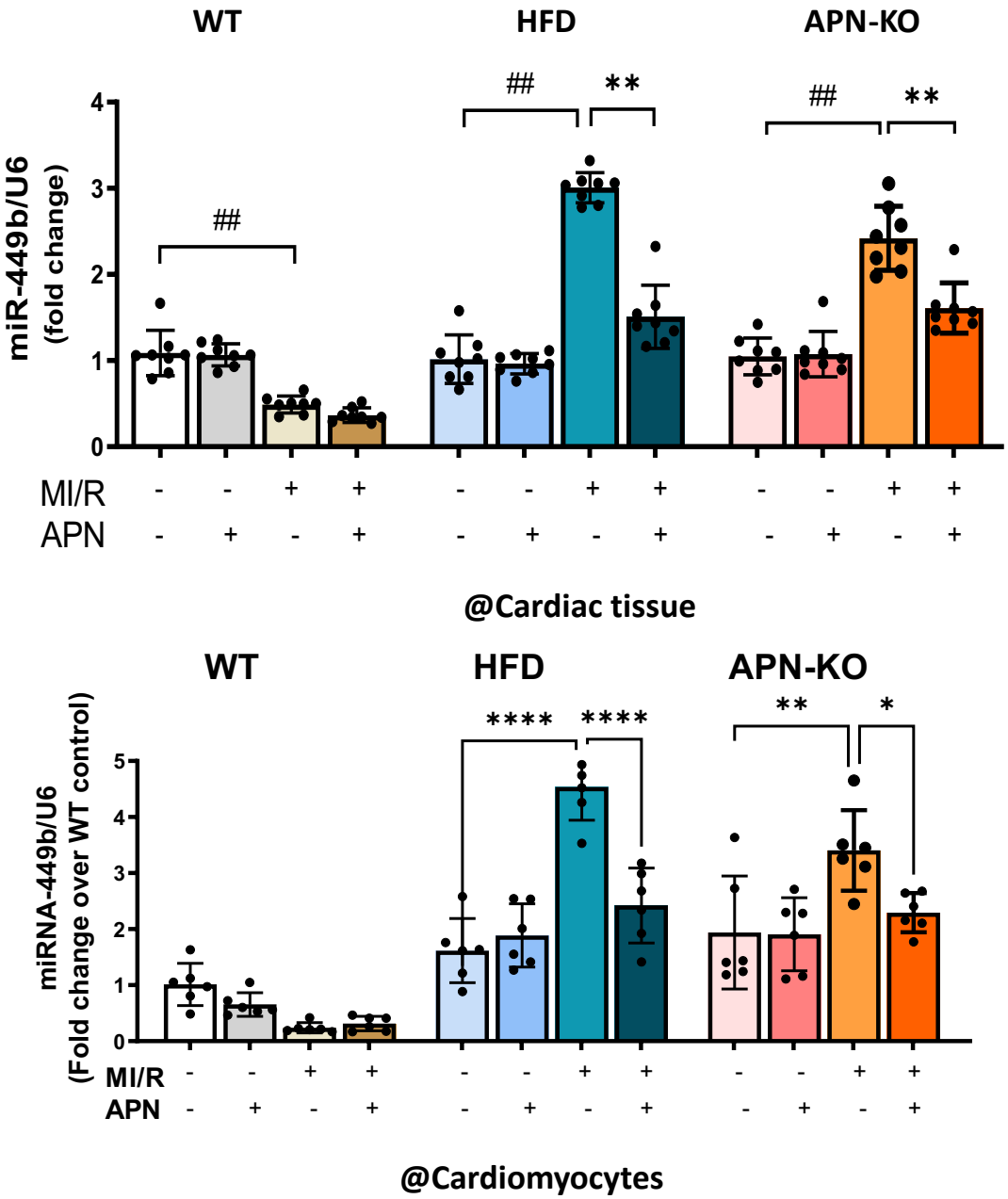
A. Administration of miR-449b mimic (miR-449b OE) significantly attenuated cardiac function in WT mice subjected to MI/R (30 minutes ischemia and 72 hours reperfusion). LVEF, left ventricle ejection fraction; FS, fraction shortening.

B. The cardiac function was significantly increased in anti-miR449b treated APN-KO mice following MI/R (30minutes ischemia and 72 hours reperfusion). APN-KO, adiponectin knockout.



Digital quantitative PCR validation using miRNA specific primer assays for miRNA-449b in cardiomyocytes isolated from WT, HFD and APNKO animals after MI/R surgery with or without APN administrated. *p < 0.05, **p<0.01 versus respective group. #p<0.05, ##p < 0.01 versus MI/R group. Statistical significance was evaluated by a two-way ANOVA. Post hoc pairwise tests for indicated group pairs were performed after Tukey correction. MI/R, myocardial ischemia/reperfusion. HFD, High fat diet; APN, Adiponectin.

Supplemental Figure 4



Real-Time quantitative PCR validation using miRNA specific primer assays for miRNA-449b in cardiac tissue and cardiomyocytes isolated from WT, HFD and APNKO animals after MI/R surgery with or without APN administrated. The relative fold calculation set WT control as 1. *p < 0.05, **p<0.01 versus respective group. ##p < 0.01 versus WT-MI/R group. Statistical significance was evaluated by a two-way ANOVA. Post hoc pairwise tests for indicated group pairs were performed after Tukey correction. MI/R, myocardial ischemia/reperfusion. HFD, High fat diet; APN. Adiponectin.

Supplemental Figure 5

Table1 Correlation between IHD without Diabetes and miR-449b

（multivariate regression analysis)

Variable	OR	ORCI95%	P
miR-449b	0.159	(0.004-0.964)	0.051
Sex(M/F)	5.495	(0.322-93.906)	0.239
Age(year)	1.100*	(1.001-1.209)	0.048
Number of lesion (number)	1.684	(0.616-2.859)	0.310
HDL-C(mmol/L)	0.415	(0.060-2.859)	0.372
LDL-C(mmol/L)	0.552	(0.096-3.166)	0.505