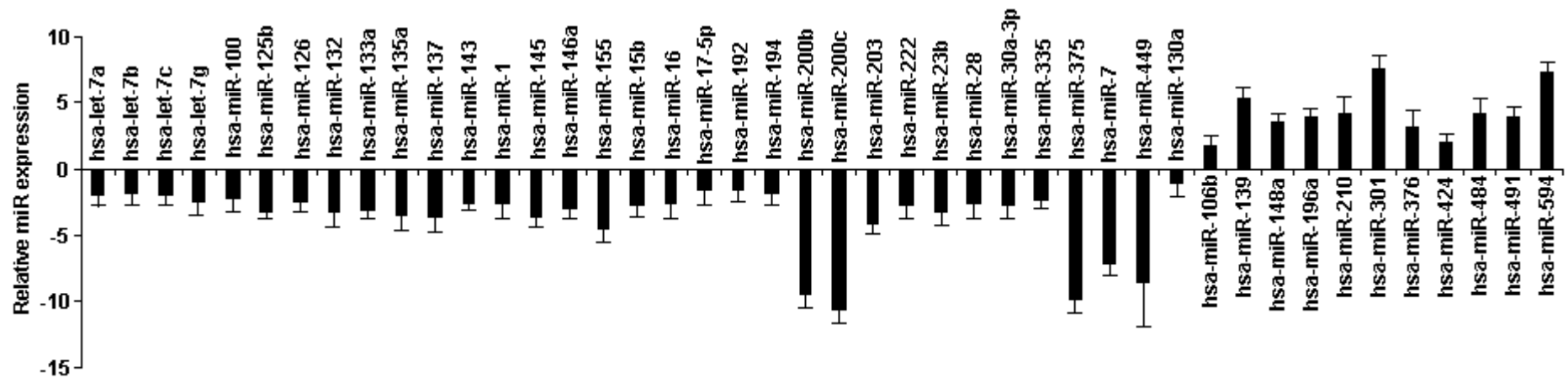
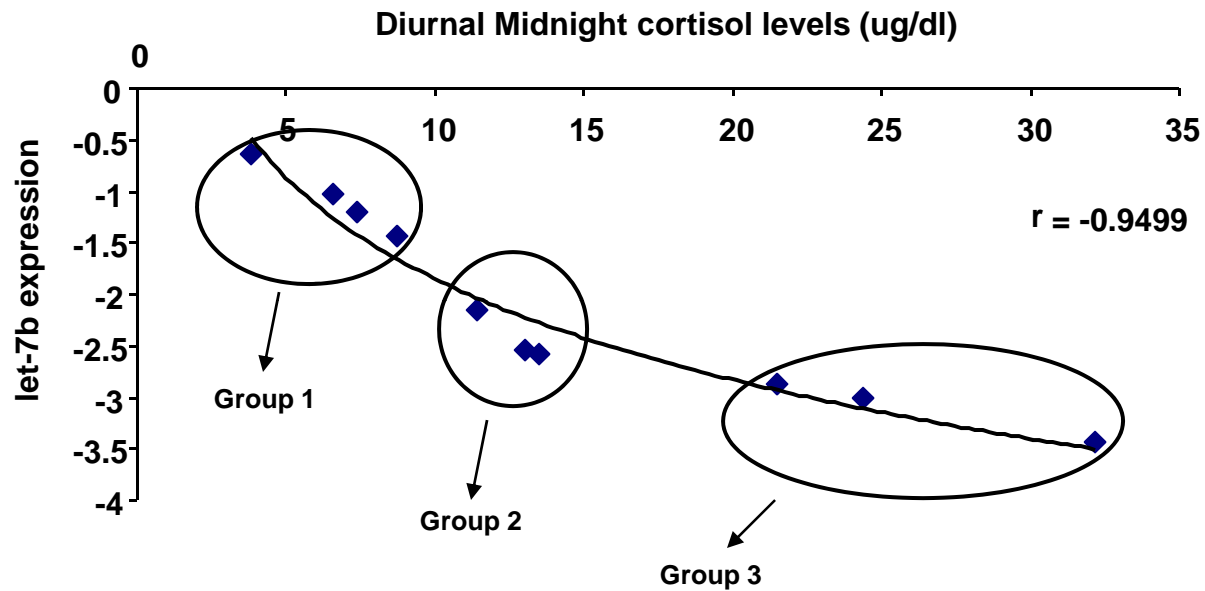


Supplementary Figure 1



Supplementary Figure 1. Real-time PCR analysis of differentially expressed microRNAs between PPNAD and normal adrenal tissues. In order to validate microRNA microarray data, we performed microRNA SYBR Green Real-time PCR analysis. The results were consistent with the microarray data, showing that 33 microRNAs were down-regulated while 11 microRNAs were up-regulated in PPNAD tissues relative to normal tissues.

Supplementary Figure 2



Supplementary Figure 2: Let-7b expression correlates with midnight cortisol levels. PPNAD patients were classified into 3 groups according to their diurnal midnight cortisol levels (low, intermediate, high); lower expression of the microRNA let-7b was associated with higher midnight cortisol levels ($r = -0.949$).

Supplementary Figure 3

Position 532-538 of FOSB 3' UTR	5' . . . UAGCUUAUUGAUCCC--ACAUUUCC				
hsa-miR-203		3'	GAUCACCAGGAUUUGUAAAGU		
Position 10-16 of INHA 3' UTR	5' . . . GGGUGGGGGGUCUUCU				
hsa-miR-7		3'	GUUGUUUUAGUGAUCAGAAGGU		
Position 152-158 of STK19 3' UTR	5' . . . AAGGUCAGAUGUGACUGCUGCUG				
hsa-miR-15b		3'	ACAUUUGGUACUAC-ACGACGAU		
Position 620-626 of CCND2 3' UTR	5' . . . UUGCUGUCUACAGUA---GUCGCUA				
hsa-miR-15b		3'	ACAUUUGGUACUACACGACGAU		
Position 87-93 of CHGA 3' UTR	5' . . . GCCAGAUGGCCCGGA--UGCUGCUU				
hsa-miR-15b		3'	ACAUUUGGUACUACACGACGAU		
Position 152-158 of STK19 3' UTR	5' . . . AAGGUCAGAUGUGACUGCUGCUG				
hsa-miR-16		3'	GCGGUUAUAAAUGCACGACGAU		
Position 1693-1699 of CCND2 3' UTR	5' . . . UUUUUUUUUUUUGCGCUCUA				
hsa-miR-16		3'	GCGGUUAUAAAUGCACGACGAU		
Position 75-82 of GPR107 3' UTR	5' . . . UUGGACAGCAGGAGCAGCUCCUA				
hsa-miR-28		3'	GAGUUAUCUGACAC-UCGAGGAA		
Position 222-228 of WISP2 3' UTR	5' . . . CCUUUCCUCUAACU---CACUGCCU				
hsa-miR-449		3'	UGGUCGAUUGUUAUGUGACGGU		

Supplementary Figure 3. Sequence complementarity between microRNAs and their target genes. TargetScan prediction algorithm identified potential microRNA-gene target pairs according to sequence similarity between the 3'UTR of a target gene and the mature sequence of a microRNA.

Supplementary Figure 4

microRNA	Gene Target	Correlation coefficient
miR-449	WISP2	-0.9743
miR-203	FOSB	-0.6221
miR-15b	CCND2	-0.5743
miR-16	CCND2	-0.5386
miR-7	INHA	-0.4254
miR-15b	STK19	-0.4189
miR-16	STK19	-0.4129
miR-15b	CHGA	-0.3875
miR-28	GPR107	-0.3343

Supplementary Figure 4. Correlation coefficient between microRNA and gene target expression. The previous analysis identified nine potential microRNA-gene target pairs. For each microRNA and gene target we performed real-time PCR analysis in order to identify their expression levels in PPNAD tissues. Due to the fact that microRNAs are negative regulators of gene expression, we were interested in the microRNA-gene target pairs with very high inversely correlated expression levels. In the table above we present the correlation coefficient between microRNA and gene target expression levels, starting from the most significant.