

Figure S1. Normalized microRNA expression profiling of samples in GSE57969.

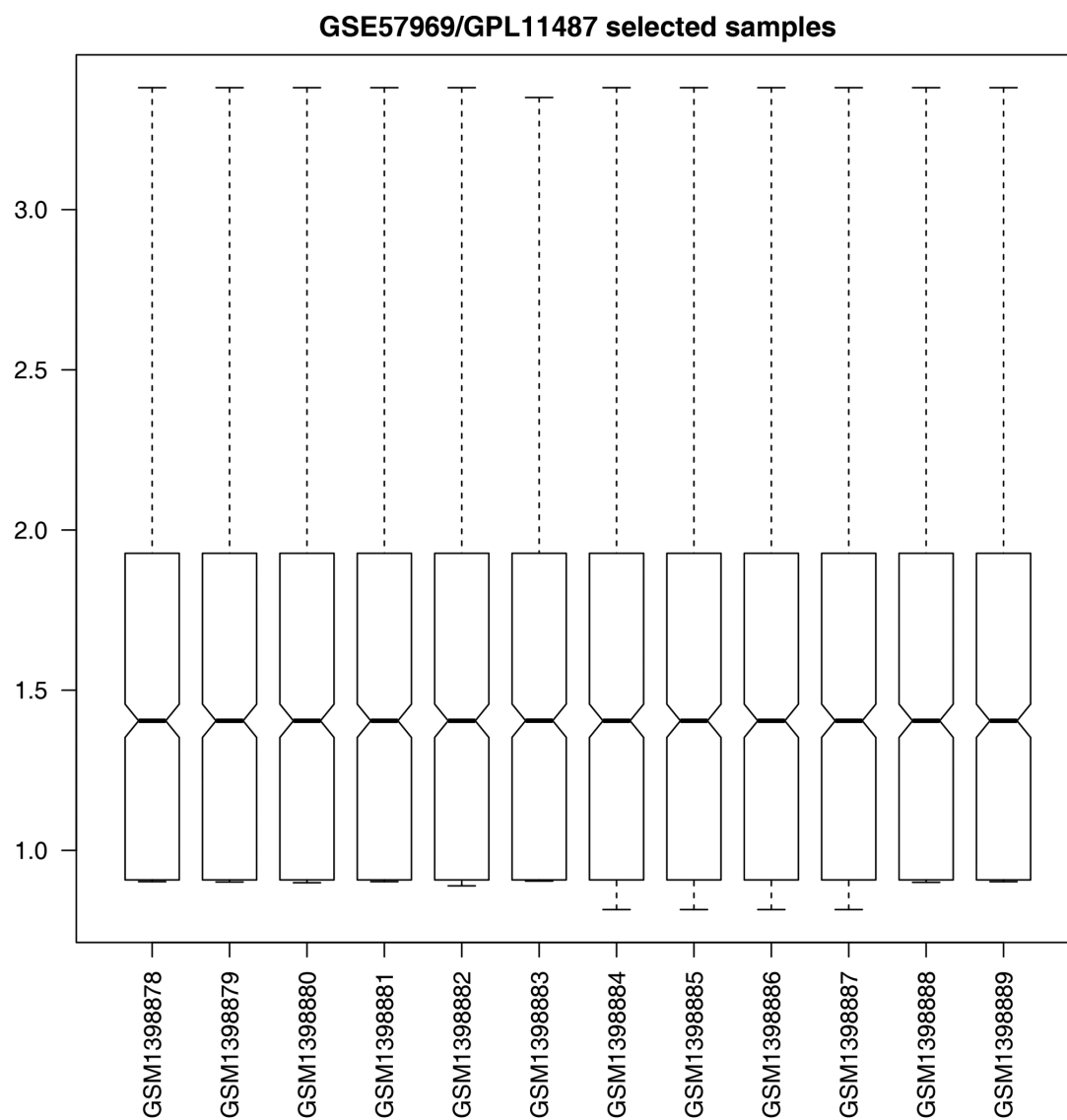


Figure S2. Workflow of the bioinformatics analysis for GSE57969. miRNA, microRNA; GO, Gene Ontology; KEGG, Kyoto Encyclopedia of Genes and Genomes; PPI, Protein-Protein Interaction; MCODES, molecular complex detection; WGCNA, weighted gene correlation network analysis.

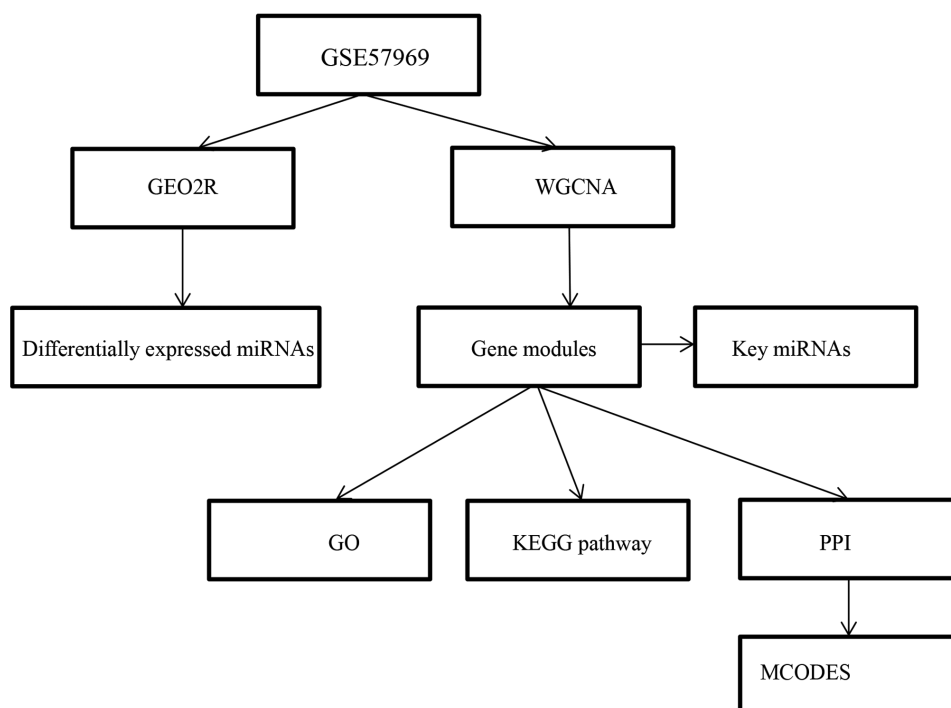


Figure S3. Volcano plot of selected miRNAs with $P < 0.05$. miR/miRNAs, microRNA.

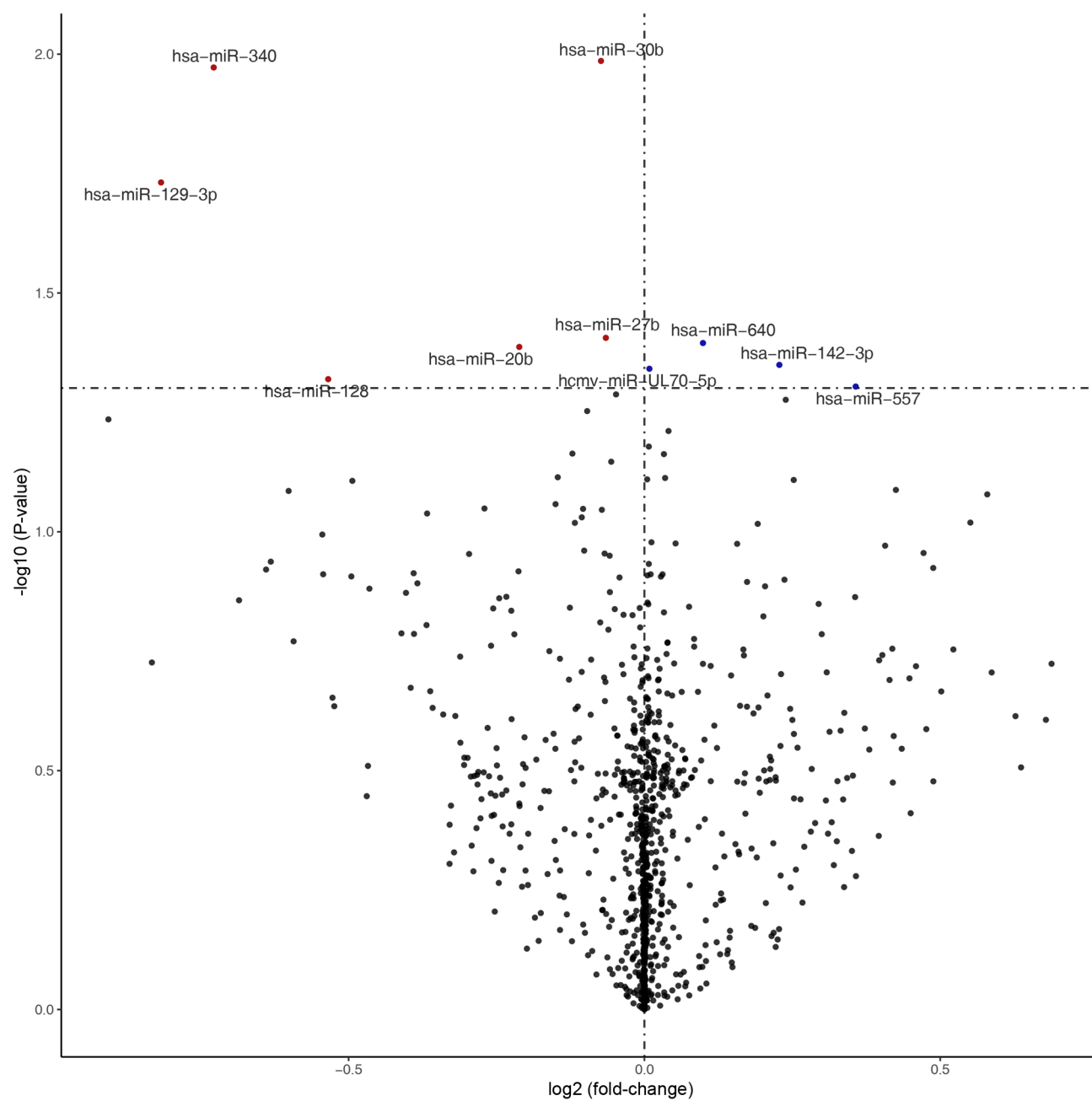


Figure S4. Heatmap of selected miRNAs with $P < 0.05$. miRNA/miR, microRNA; STC, slow-transit constipation.

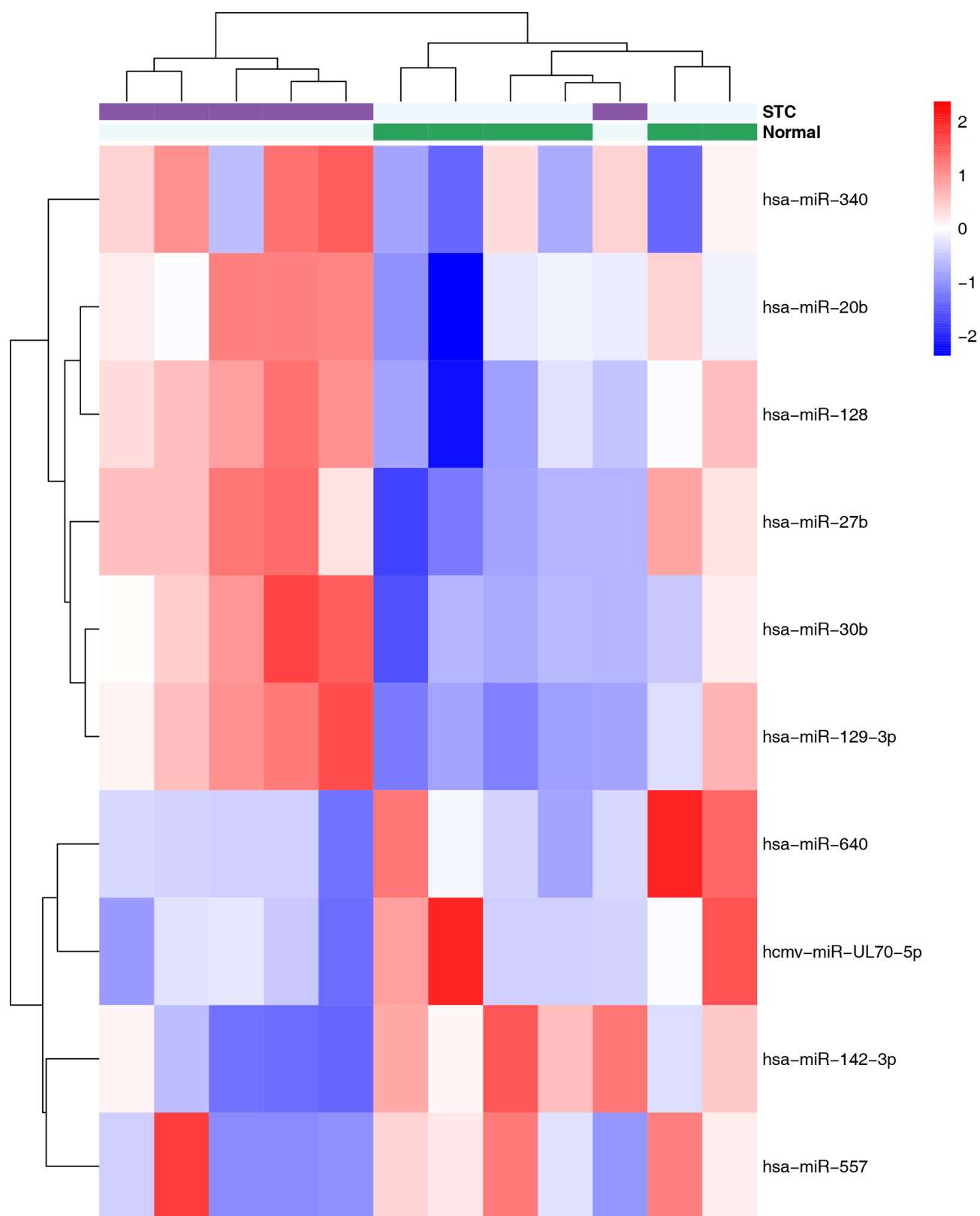


Table SI. Information on the included samples.

A, STC sample		
Sample ID	Gender	Description
GSM1398879	Female	Full-thickness colonic specimen
GSM1398881	Female	Full-thickness colonic specimen
GSM1398883	Female	Full-thickness colonic specimen
GSM1398885	Female	Full-thickness colonic specimen
GSM1398887	Female	Full-thickness colonic specimen
GSM1398889	Male	Full-thickness colonic specimen
B, Normal colon sample		
Sample ID	Gender	Description
GSM1398878	Female	Full-thickness colonic specimen
GSM1398880	Female	Full-thickness colonic specimen
GSM1398882	Female	Full-thickness colonic specimen
GSM1398884	Female	Full-thickness colonic specimen
GSM1398886	Female	Full-thickness colonic specimen
GSM1398888	Male	Full-thickness colonic specimen
STC, slow-transit constipation.		

Table SII. Differentially expressed miRNAs between normal and STC groups based on the GEO2R web tool.

miRNA ID	P-value	LogFC	Expression in STC compared with normal
hsa-miR-557	0.0496	3.57×10^{-1}	Upregulated
hsa-miR-154	0.0529	2.39×10^{-1}	Upregulated
hsa-miR-142-3p	0.0447	2.28×10^{-1}	Upregulated
hsa-miR-640	0.0402	9.90×10^{-2}	Upregulated
jcv-miR-J1-5p	0.0615	4.07×10^{-2}	Upregulated
bkv-miR-B1-3p	0.0688	3.30×10^{-2}	Upregulated
hcmv-miR-UL70-5p	0.0456	8.42×10^{-3}	Upregulated
hsa-miR-30d	0.0663	7.45×10^{-3}	Upregulated
hsa-miR-29c	0.0516	-4.8×10^{-2}	Downregulated
hsa-miR-324-3p	0.0713	-5.6×10^{-2}	Downregulated
hsa-miR-27b	0.0393	-6.5×10^{-2}	Downregulated
hsa-miR-30b	0.0103	-7.3×10^{-2}	Downregulated
hsa-miR-30e	0.0559	-9.6×10^{-2}	Downregulated
hsa-miR-361-5p	0.0686	-1.2×10^{-1}	Downregulated
hsa-miR-320a	0.0769	-1.4×10^{-1}	Downregulated
hsa-miR-20b	0.041	-2.1×10^{-1}	Downregulated
hsa-miR-128	0.0479	-5.3×10^{-1}	Downregulated
hsa-miR-340	0.0107	-7.2×10^{-1}	Downregulated
hsa-miR-129-3p	0.0186	-8.1×10^{-1}	Downregulated
hsa-miR-490-3p	0.0582	-9.0×10^{-1}	Downregulated

miR/miRNA, micro RNA; STC, slow-transit constipation; FC, fold-change.

Table SIII. Key miRNAs with the highest correlation to STC.

miRNA_ID	moduleColorsFemale	cor.gender	cor.STC
hsa-miR-619	blue	-0.08368	0.691847
hsa-miR-20b	turquoise	0.234427	-0.60402
hsa-miR-128	turquoise	0.382428	-0.61819
hsa-miR-486-3p	black	0.143986	-0.64059
hsa-miR-129-3p	turquoise	0.536344	-0.64954
hsa-miR-30b	turquoise	0.385572	-0.69318
hsa-miR-340	turquoise	0.371688	-0.70344

miR/miRNA, microRNA; STC, slow-transit constipation; cor, correlation.

Table SIV. Alternative functional pathway enrichment from the BioCarta database.

Term	Count	Ratio of genes to total genes in the pathway (%)	P-value	Genes	FDR
h_metPathway:Signaling of Hepatocyte Growth Factor Receptor	11	0.559512	0.016736	CRKL, SOS1, RAP1A, ELK1, RAP1B, MAPK8, PAK1, CRK, PIK3R1, RASA1, STAT3	19.74355
h_mapkPathway:MAPKinase Signaling Pathway	20	1.017294	0.018616	MEF2C, CREB1, TGFBRI, RELA, MKNK2, MAPKAPK3, ELK1, RPS6KA5, MAP3K5, MAP4K5, SPI, RPS6KA2, MAP3K2, MAP3K9, MAP3K1, MAPK9, MAPK8, PAK1, MAP2K7, MAP3K12	21.71998
h_egfPathway:EGF Signaling Pathway	9	0.457782	0.021383	PRKCA, SOS1, MAP3K1, JAK1, ELK1, MAPK8, PIK3R1, RASA1, STAT3	24.54806
h_at1rPathway:Angiotensin II mediated activation of	10	0.508647	0.02569	PRKCA, MEF2C, GNAQ, SOS1, MAP3K1, ELK1, MAPK8, PAK1, CALM2, CALM1	28.76304
JNK Pathway via Pyk2 dependent signaling	9	0.457782	0.026562	PRKCA, SOS1, MAP3K1, JAK1, ELK1, MAPK8, PIK3R1, RASA1, STAT3	29.58922
h_pdgfPathway:PDGF Signaling Pathway	9	0.457782	0.026562	PRKCA, CRKL, GNAQ, SOS1, MAP3K1, MAPK8, PAK1, CALM2, CALM1	29.58922
h_pyk2Pathway:Links between Pyk2 and Map Kinases	12	0.610376	0.026975	PRKCA, RELA, SOS1, MAP3K1, ELK1, MAPK8, NFATC2, NFATC3, PIK3R1, RASA1, CALM2, CALM1	29.97687
h_tcrPathway:T Cell Receptor Signaling Pathway	11	0.559512	0.029043	LYN, SOS1, MAP3K1, ELK1, MAPK8, NFATC2, MAP2K7, NFATC3, PIK3R1, CALM2, CALM1	31.89224
h_bcrPathway:BCR Signaling Pathway	10	0.508647	0.03097	PRKCA, LYN, SOS1, MAP3K1, ELK1, MAPK8, NFATC2, NFATC3, CALM2, CALM1	33.63229
h_calcineurinPathway:Effects of calcineurin in Keratinocyte Differentiation	7	0.356053	0.033096	PRKCA, SP1, GNAQ, NFATC2, NFATC3, CALM2, CALM1	35.50506
h_vipPathway:Neuropeptides VIP and PACAP inhibit the apoptosis of activated T cells	8	0.406918	0.050301	EGR2, GNAQ, RELA, MAP3K1, NFATC2, VIPR2, CALM2, CALM1	48.9596
h_pkcPathway:Activation of PKC through G protein coupled receptor	4	0.203459	0.055836	PRKCA, GNAQ, RELA, PLCB1	52.70312
h_tubbyPathway:G-Protein Signaling Through Tubby Proteins	4	0.203459	0.080672	GNAQ, RIC3, PLCB1, HTR2C	66.58294
h_ctbp1Pathway:SUMOylation as a mechanism to modulate CtBP-dependent gene responses	4	0.203459	0.080672	SUMO1, NOS1, UBE2I, ZEB1	66.58294

Table SIV. Continued.

Term	Count	Ratio of genes to total genes in the pathway (%)	P-value	Genes	FDR
h_PDZsPathway:Synaptic Proteins at the Synaptic Junction	6	0.305188	0.083029	NCAM1, EPB41, NFASC, SPTBN1, DLG2, DLG1	67.68231
h_cardiacEGFPathway:Role of EGF Receptor Transactivation by GPCRs in Cardiac Hypertrophy	6	0.305188	0.083029	PRKCA, EDNRA, EDNRB, RELA, RHOA, ADAM12	67.68231
h_CaCaMPathway:Ca++/Calmodulin-dependent Protein Kinase Activation	5	0.254323	0.085646	CREB1, CAMK2D, CALM2, CAMKK2, CALM1	68.86382
FDR, false discovery rate.					

Table SV. Target hub genes in association with key miRNAs.

Key miRNA	Target hub genes
hsa-miR-619	CALM2, HDAC3, GNG7
hsa-miR-20b	HSPA8
hsa-miR-128	GSK3B, GNG13
hsa-miR-486-3p	-
hsa-miR-129-3p	-
hsa-miR-30b	GSK3B, HDAC9, HACE1, GNG10
hsa-miR-340	CALM1

miRNA/miR, microRNA; CALM, Calmodulin; HDAC, histone deacetylase; GNG, G-protein subunit γ ; HSPA8, heat-shock protein family A member 8; GSK3B, glycogen synthase kinase 3 β ; HACE, HECT domain and ankyrin repeat containing E3 ubiquitin protein ligase 1.

Table SVI. Topological features of the top 20 genes identified from Protein-Protein Interaction networks.

Name	Average Shortest Path Length	Betweenness Centrality	Degree	Closeness Centrality	Clustering Coefficient	Neighborhood Connectivity	Radiality	Topological Coefficient
CALM2	2.46548957	0.113863	55	0.405599	0.091582	16.49091	0.866774	0.046533
CALM1	2.52487961	0.096835	52	0.396058	0.100302	17.03846	0.861375	0.051167
HDAC3	2.78651685	0.048074	42	0.358871	0.175377	16.47619	0.837589	0.069028
GSK3B	2.66613162	0.075369	41	0.375075	0.10122	16.82927	0.848533	0.061199
HDAC9	2.72552167	0.059312	41	0.366902	0.154878	16.78049	0.843134	0.068654
HSPA8	2.6918138	0.100115	41	0.371497	0.112195	15	0.846199	0.056693
GNGI3	3.18619583	0.013093	40	0.313854	0.364103	19.55	0.801255	0.143566
HACE1	2.86035313	0.044091	39	0.349607	0.269906	19.30769	0.830877	0.091453
GNGI0	3.14446228	0.019409	39	0.318019	0.376518	19.17949	0.805049	0.137613
GNG7	3.29855538	0.005435	38	0.303163	0.40256	18.76316	0.79104	0.169037
ACTR1A	2.68699839	0.072237	38	0.372162	0.11522	17.34211	0.846637	0.064317
DLG1	2.83467095	0.041666	37	0.352775	0.10961	14.45946	0.833212	0.066692
GNB5	3.31139647	0.004296	35	0.301987	0.458824	19.94286	0.789873	0.184656
ACTC1	2.8105939	0.042335	33	0.355797	0.106061	16.27273	0.835401	0.072428
CREB1	2.72070626	0.044781	33	0.367552	0.174242	19.72727	0.843572	0.075179
DLG2	2.85874799	0.036994	33	0.349803	0.147727	16.21212	0.831023	0.076329
ABL1	2.68378812	0.067529	31	0.372608	0.137634	19.70968	0.846928	0.072372
AR	2.78651685	0.042805	31	0.358871	0.107527	17.35484	0.837589	0.073063
CUL2	3.2600321	0.024628	30	0.306745	0.4	16.03333	0.794543	0.159259
GNAI2	3.48796148	0.005382	30	0.2867	0.45977	19.56667	0.773822	0.219476

Table SVII. Topological table of the Molecular Complex Detection from the Protein-Protein Interaction networks.

Cluster	Score	Nodes	Edges	Node IDs
1	19.053	39	362	HACE1, GNG7, KLHL2, GNB5, GNAI2, GRM2, GRM3, GABBR2, KLHL20, GAN, ASB7, CXCL6, ASB8, KLHL25, APLN, APLNR, ITCH, CBLB, FBXL3, HECTD1, FBXO30, GNG10, GNG13, CNR1, HECTD2, CUL2, ADORA1, FBXL20, HRH3, CCL28, CCL16, HTR1D, HERC3, HECW2, BDKRB2, FBXO41, FBXO32, KLHL13, ADCY2
2	11	11	55	HNRNPU, GCFC2, CPSF7, DDX5, CDC5L, HNRNPA3, CWC25, CLP1, CPSF2, HSPA8, HNRNPA0
3	10	11	50	HDAC9, HDAC3, KAT6A, H3F3C, ARID4A, ARID4B, CHD3, CECR2, ASF1B, H3F3B, INO80