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Identifying microRNA-Target Gene Pairs in Luminal B Breast Cancer Using Integrated Analysis of miRNA and Transcriptome Profiles

Kayalvili Ulaganathan, Raviteja Reddy Alipeddi, Surekha Rani Hanumanth*

Department of Genetics, Osmania University, Hyderabad, Telangana, India
Email: *surekharanih@osmania.ac.in

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Abstract

Dysregulation of post-transcriptional regulation of gene expression has been found to influence various human disorders. Aberrant miRNA-based regulation of gene expression has been found to be associated with different cancers, including breast cancers. Very little information is available on the effect of dysregulation of miRNA-mediated regulation on luminal B breast cancer. This study was aimed at comprehending the regulation of gene expression through miRNA in luminal B breast cancers by comprehensive analysis of miRNA and mRNA expression data together. Negatively regulated miRNA-target gene pairs were identified, and the target genes were functionally enriched to identify critical pathways associated with luminal B breast cancer. Further, the prognostic significance of these miRNAs and target gene pairs was assessed to identify genes with prognostic value in luminal B breast cancer. A total of 266 differentially expressed miRNAs and 164 dysregulated miRNA-target gene pairs were identified. Four genes, including SRP9, DSN1, RACGAP1, and SLC10A6, and one miRNA, hsa-mir-421, showed significant influence on the prognosis of patients with luminal B breast cancer. Through additional experimental examination of these findings, a deeper comprehension of miRNA-based post-transcriptional regulation in luminal B breast tumors will be possible.

Keywords

Breast Cancer, Luminal B, miRNA, mRNA, TCGA

1. Introduction

According to GLOBOCAN 2022, female breast cancer accounts for an estimated 11.6% of all cancer cases worldwide, making it the second most common cause of

cancer incidence [1]. Breast cancer most commonly originates from the epithelial cells lining the milk ducts and is of 4 main subtypes: Luminal A, Luminal B, Her2-enriched, and Basal-like [2] [3]. Post-transcriptional regulation influences cell-specific expression patterns by controlling RNA processing, localization, translation, and destruction [4] [5]. MicroRNAs are small, non-coding RNAs that have a length of about 21 nucleotides. They play a major role in regulating gene expression post-transcriptionally. Depending on the degree of complementarity with target mRNA sequences in the 3'UTR, the miRNA/mRNA interaction results in either repression of translation or degradation of mRNA [6]. It has been reported that dysregulation of miRNA expression is linked to breast cancer. Tumor suppressor miRNA (tsmiR) or oncogenic miRNA (oncomiR) regulates different biological processes involved in the development of breast cancer, including apoptosis, metastasis, cancer recurrence, and cell proliferation [7] [8].

Luminal B breast cancers are an aggressive and highly proliferative subtype of breast cancer [9]. The miR-99a/let-7c/miR-125b cluster has been identified to be a marker for distinguishing luminal A from luminal B subtype, with a lower expression of this cluster of miRNAs in luminal B breast cancer [10]. Also, the luminal B subtype showed a distinct expression pattern of miR-182-5p, miR-200b-3p, miR-15b-3p, miR-149-5p, miR-193b-3p and miR-342-3p, 5p [11]. While there are a few miRNA-based studies on the luminal B breast cancer subtype, there aren't a lot of studies that analyze both the miRNA and the mRNA expression data together. Comprehending the regulation of gene expression through miRNAs plays a pivotal role in understanding the unique expression patterns observed in breast cancers. Our earlier analysis concentrated on identifying luminal B specific expression patterns [12]. In this study, we investigated the post-transcriptional regulation of gene expression by analyzing both miRNA and mRNA expression data together to identify critical miRNA-target gene pairs in luminal B breast cancer.

2. Methods

2.1. Data Collection

Luminal B breast cancer sample expression data and clinical data were obtained from TCGA (The Cancer Genome Atlas). Both miRNA and mRNA expression data of 164 inflammatory ductal carcinoma luminal B breast cancer samples, including 16 paired normal samples, were retrieved. The samples that had both mRNA expression data and miRNA expression data were only included. cBioPortal was used to obtain the PAM50 subtype classification data (cBioportal. https://www.cbioportal.org/).

2.2. Differential Expression of mRNA and miRNA in Luminal B Breast Cancer

The miRNA and mRNA expression data retrieved were used for differential expression analysis. The differential expression of miRNA and mRNA between the

luminal B tumor samples and corresponding normal samples was analyzed using DEseq2, a tool that tests for differential expression by use of negative binomial generalized linear models [13]. The count data was imported into DEseq2, normalized, and the differential expression was quantified as log2 fold change (logFC) values. The wald test was used to assess the statistical significance and corrected for by Benjamini & Hochberg method. The miRNA and mRNA that were differentially expressed with a $|\log FC| \geq 1$ and FDR < 0.05 were considered significant. Principal component analysis (PCA) was carried out in R. Heatmaps of top 100 differentially expressed miRNA and mRNA was generated using pheatmap function. Volcano plots were generated using ggplot2.

2.3. Identification of Dysregulated miRNA-Target Gene Pairs in Luminal B Breast Cancer

Firstly, miRTarBase, a database that contains experimentally validated target sites of miRNAs, was used to identify all the target mRNAs of miRNAs differentially expressed in luminal B breast cancer [14]. The target mRNAs that were identified to be differentially expressed in luminal B breast cancer in our analysis were only retained. The differentially expressed miRNA and mRNA that showed opposite trends of expression were used to identify miRNA-target gene pairs. These miRNA-mRNA pairs were further analyzed for correlation between normalized mRNA expression values and normalized miRNA expression values using the Spearman correlation method. The miRNA-target gene pairs that showed a negative correlation were only considered. A cutoff of Spearman's correlation coefficient (R) < −0.2 and p < 0.05 was used to identify significant pairs.

2.4. Functional Annotation and miRNA-Target Gene Pair Visualization

The differentially expressed target genes were functionally enriched using Enrichr in R. Enrichr is a web-based tool that is used for functional enrichment analysis of gene sets [15]. The genes were enriched for Gene Ontology (GO) terms and Kyto Encyclopedia of Genes and Genomes (KEGG) pathways. A cut-off of p-value < 0.05 was used to identify the significant pathways enriched. Also, the significant miRNA-target gene pairs were visualized using cytoscape, a tool for visualization and integration of molecular interaction networks with gene expression data [16].

2.5. Survival Analysis

Kaplan-Meier survival method was used to investigate the correlation between gene expression and overall survival (OS). Survival analysis was carried out in R. Based on median expression value, the samples were divided into high and low expression groups and the log-rank test was used to assess the statistical significance of difference in survival probabilities between the survival curves of low and high expression groups. A p value of <0.05 was used as cut-off to identify the

significant associations.

3. Results

3.1. Data Used in the Analysis

The mRNA and miRNA expression data of 164 inflammatory ductal carcinoma luminal B breast cancer samples, including 16 paired normal samples, were retrieved from TCGA. The clinical details of the patients are shown in Table 1.

Table 1. Patient clinicopathological characteristics.

	Luminal B, n (%)
Age (years)	
<60	88 (53.66%)
≥60	76 (46.34%)
Sex	
Female	164 (100%)
Male	0 (0%)
Stage	
I	17 (10.37%)
II	89 (54.27%)
III	52 (31.70%)
IV	4 (2.44%)
N/A	2 (1.22%)

3.2. Differential mRNA Expression in Luminal B Breast Cancer

Differential expression of mRNA between 164 luminal B breast cancer and 16 paired normal tissue samples identified 5951 significant differentially expressed mRNAs ($|\log FC| \geq 1$ and FDR < 0.05). Of the 5951 differentially expressed mRNAs, 2972 were down-regulated and 2979 were up-regulated between luminal B breast cancer and corresponding surrounding normal tissue samples. PCA analysis using mRNA expression data showed differential clustering of tumor and normal samples. PCA analysis was carried out on the log2 transformed gene expression data, where the principal component 1 (PC1) accounted for 14% of the total variance and principal component 2 (PC2) accounted for 9% the total variance (Figure 1(a)). Heatmap of top 100 differentially expressed genes between luminal B breast cancer tissues and paired normal tissue samples was generated using pheatmap (Figure 1(b)) and a volcano plot of differentially expressed mRNAs between the tumor tissue and paired normal tissue samples is shown in Figure 1(c).

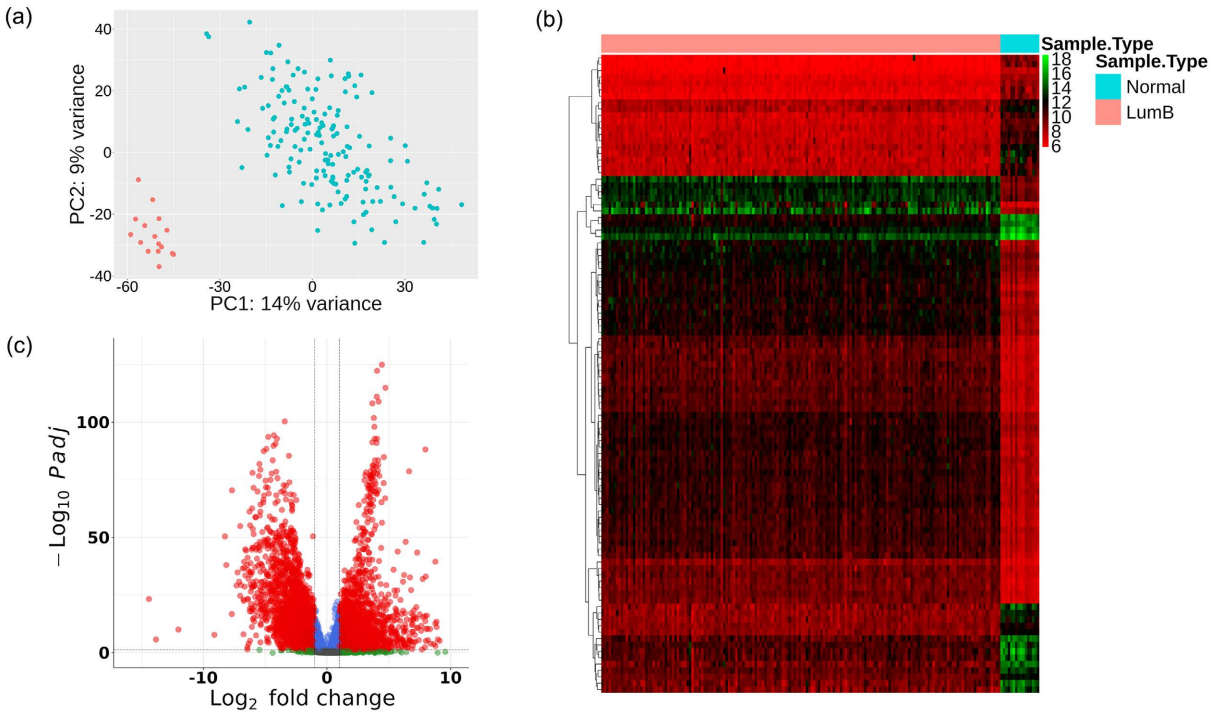


Figure 1. Differential expression of mRNA in luminal B breast cancer. (a) Principal component analysis using mRNA expression data. Blue dots represent luminal B tumor samples; Red dots represent paired normal samples; PC1 represents principal component 1; PC2 represents principal component 2. (b) Heatmap of top 100 differentially expressed genes. LumB represents Luminal B subtype. (c) Volcano plot of differentially expressed mRNA. X axis represents log2 (fold change); Y axis represents −log10 (FDR); Red dots represent genes with significantly differential expression.

3.3. Differential miRNA Expression in Luminal B Breast Cancer

Differential miRNA expression analysis between 164 luminal B breast cancer and 16 paired normal tissue samples identified 266 significant differentially expressed miRNAs. Of the 266 differentially expressed miRNAs, 117 were down-regulated and 149 were up-regulated between luminal B breast cancer and the corresponding surrounding normal tissue samples (Supplementary Table S1). PCA analysis using miRNA expression data showed differential clustering of tumor and normal samples. PCA analysis was carried out on the log2 transformed miRNA expression data, where the PC1 accounted for 12% of the total variance and PC2 accounted for 5% the total variance (Figure 2(a)). Heatmap of top 100 differentially expressed miRNA between luminal B breast cancer tissues and paired normal tissue samples was generated using pheatmap (Figure 2(b)) and a volcano plot of differentially expressed miRNAs between the tumor tissue and paired normal tissue samples is shown in Figure 2(c).

3.4. Critical Dysregulated miRNA-Target Gene Pairs

The miRTarBase, containing experimentally validated miRNA target sites, was searched for the identification of target sites of differentially expressed miRNAs. Differentially expressed miRNAs and mRNAs that showed opposite trends of expression were used for identifying the miRNA-mRNA pairs. Further, these

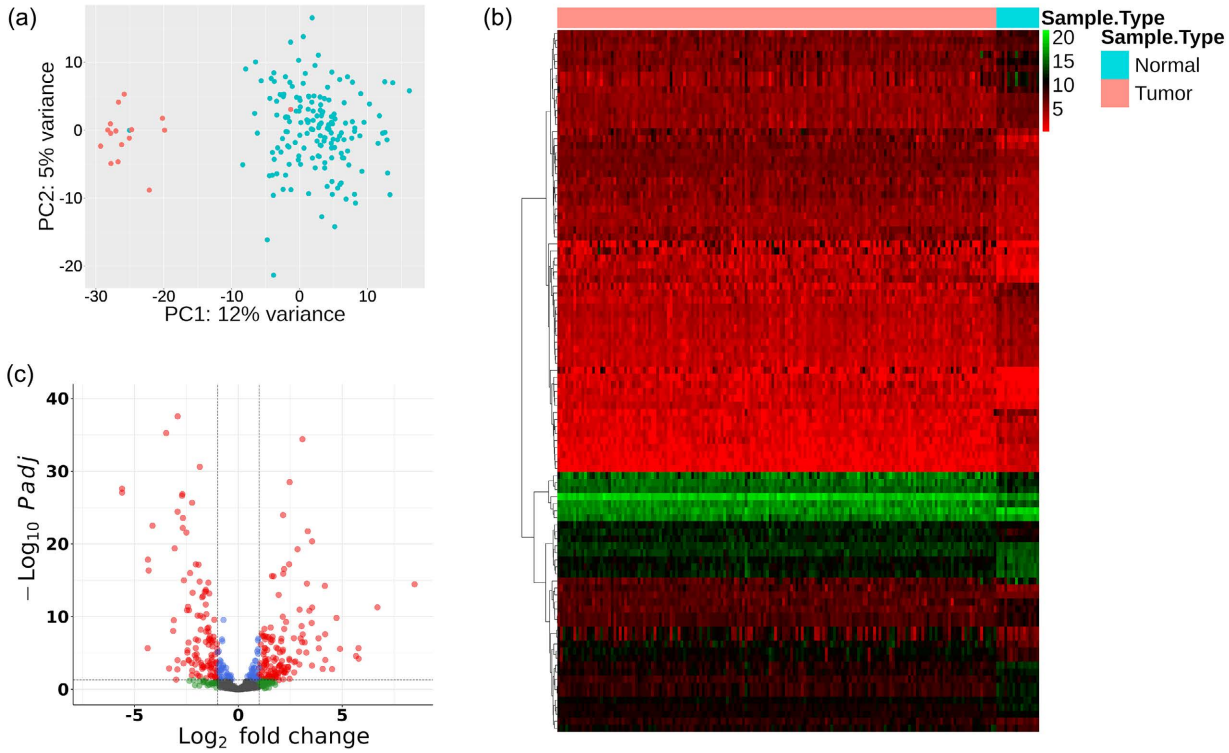


Figure 2. Differential expression of miRNA in luminal B breast cancer. (a) Principal component analysis using miRNA expression data. The Blue dots represent luminal B tumor samples; Red dots represent paired normal samples; PC1 represents principal component 1; PC2 represents principal component 2. (b) Heatmap of top 100 differentially expressed miRNAs. LumB represents Luminal B subtype. (c) Volcano plot of differentially expressed miRNA. X axis represents $\log_2$ (fold change); Y axis represents $-\log_{10}$ (FDR); Red dots represent genes with significantly differential expression.

miRNAs and targets were analyzed for correlation using the Spearman correlation method. The miRNA-target gene pairs that showed a negative correlation with Spearman's correlation coefficient $R < -0.2$ and p-value < 0.05 were considered significant. This led to the identification of 164 significant miRNA-target gene pairs, which include 31 miRNAs and 154 mRNAs (Supplementary Table S2; Supplementary Table S3). The miRNA-mRNA regulatory pairs were visualized using cytoscape (Figure 3).

3.5. Functional Enrichment of Target mRNAs

The differentially expressed target genes were enriched for pathways using Enrichr in R. Using a p value cut-off of 0.05, genes were enriched for GO terms and KEGG pathways (Figure 4). The top KEGG pathways enriched among the target genes were pathways in cancer, the Ras signaling pathway, focal adhesion, and the PI3K-Akt signaling pathway. The top GO molecular function terms enriched were transcription regulatory region DNA binding, regulatory region DNA binding, and transmembrane receptor protein kinase activity. The top GO biological process terms enriched were positive regulation of nucleic acid-templated transcription, regulation of transcription from the RNA polymerase II promoter, regulation of transcription, DNA templated, and positive regulation of gene expression.

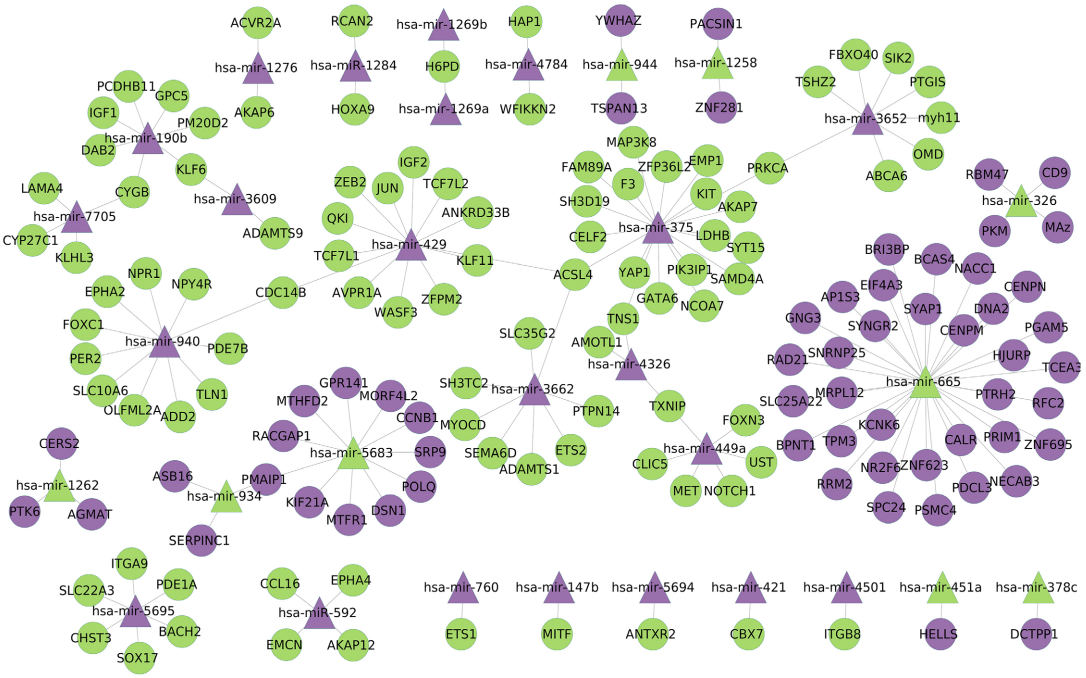
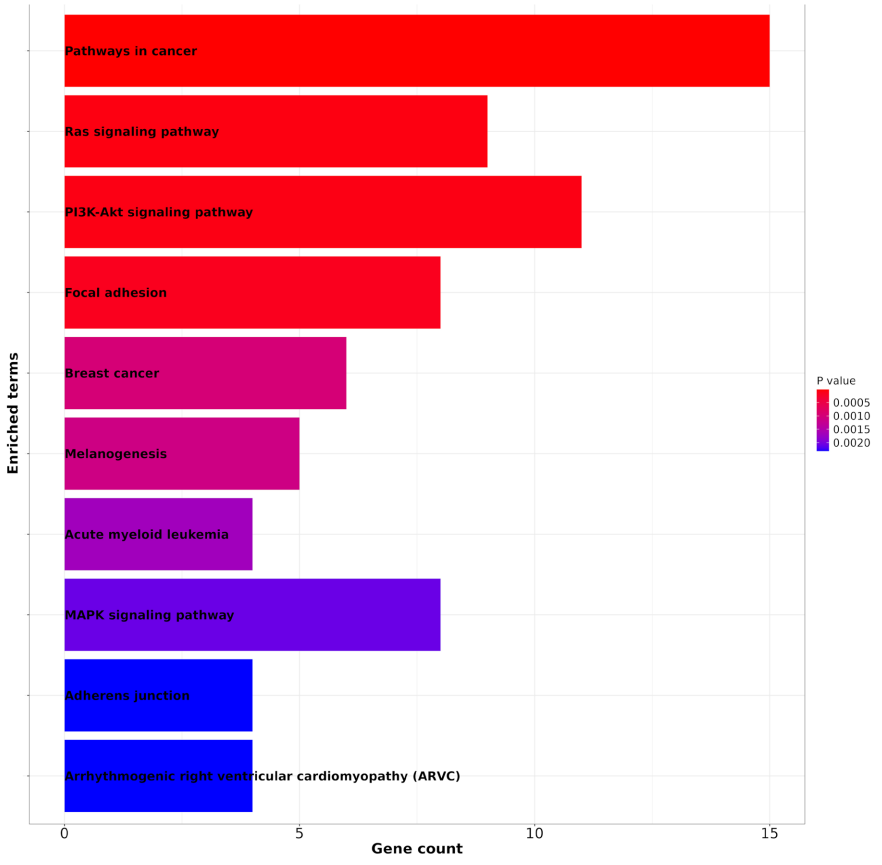
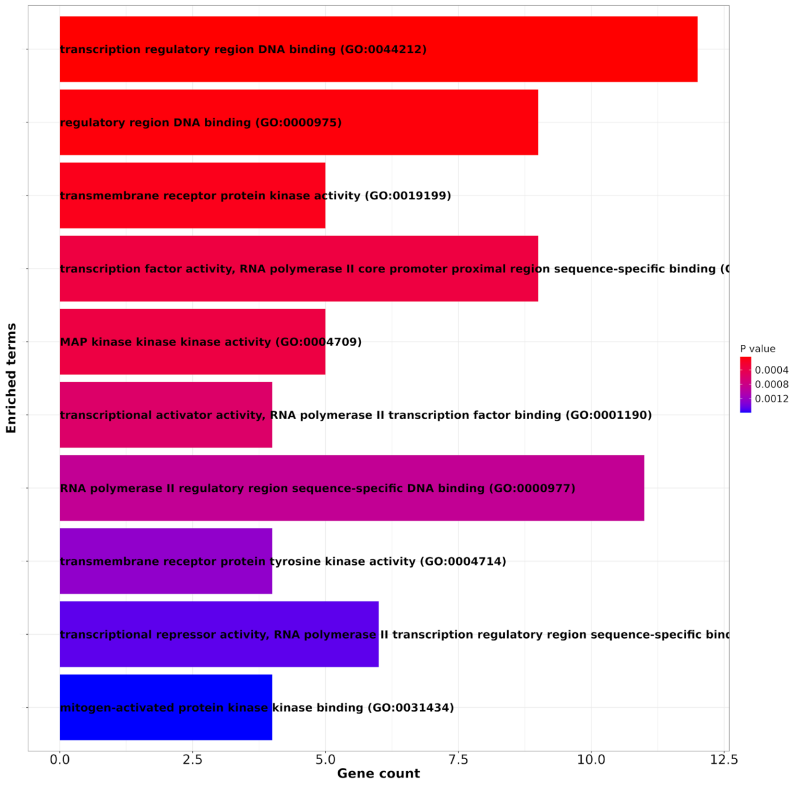


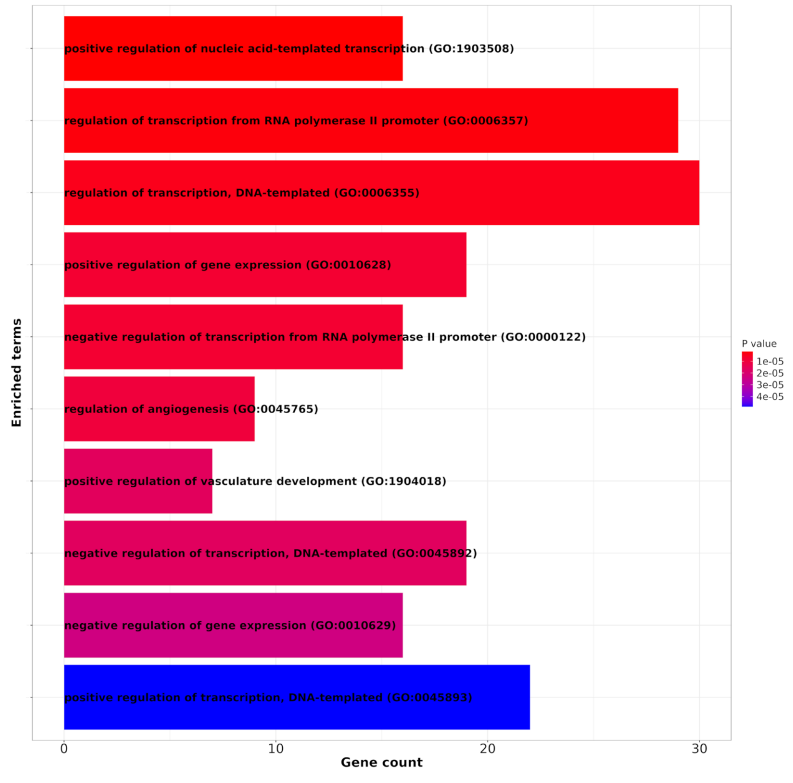
Figure 3. Network of miRNA-target gene interactions in luminal B breast cancer. The circle nodes represent mRNAs. The triangle nodes represent miRNAs; Purple colour represents over-expression and green colour represents low expression; edges represent the correlation between the miRNA and mRNA expression.



(a)



(b)



(c)

Figure 4. Functional enrichment analysis of 154 target genes (a) KEGG pathway, (b) GO molecular function and (c) GO Biological process terms enriched.

3.6. Survival Analysis

To further elucidate the roles of 164 miRNA target gene pairs, the miRNAs and target genes identified were analyzed using the Kaplan-Meier method to investigate the association of expression with survival time. This resulted in the identification of five genes, including miR-421, DSN1 (DSN1 Component Of MIS12 Kinetochore Complex), SRP9 (Signal Recognition Particle 9), RACGAP1 (Rac GTPase Activating Protein 1), and SLC10A6 (Solute Carrier Family 10 Member 6), that had prognostic value. Expression of miRNA hsa-mir-421 was found to be up-regulated in luminal B breast cancers, and was negatively correlated with its target gene CBX7. Higher expression of this miRNA in luminal B breast cancers was associated with poor survival. Target genes DSN1, SRP9 and RACGAP1 were found to be overexpressed in luminal B breast cancers, and their expression was significantly negatively correlated with the expression of miRNA hsa-mir-5683. The up-regulation of DSN1, SRP9 and RACGAP1 was found to be associated with poor survival. Expression of genes SLC10A6 was down-regulated in luminal B breast cancers, and was significantly negatively correlated with the expression of hsa-mir-940. Lower expression of this gene was found to be associated with poor survival. Survival plots showing survival curves of low and high expression groups, and scatter plots of Spearman correlation analysis for the prognostic genes are shown in Figure 5 and Figure 6, respectively.

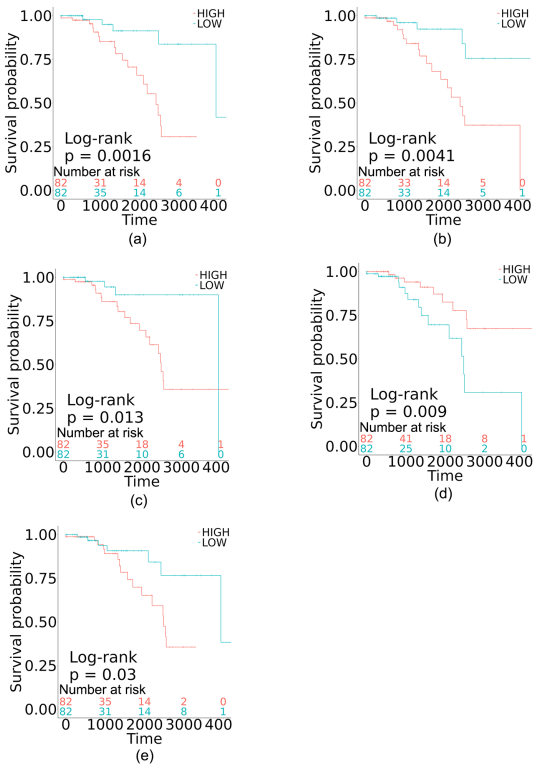


Figure 5. Survival analysis of luminal B breast cancer patients. Kaplan-Meier survival curves showing association between expression of (a) DSN1, (b) SRP9, (c) RACGAP1, (d) SLC10A6, (e) hsa-mir-421 and overall survival.

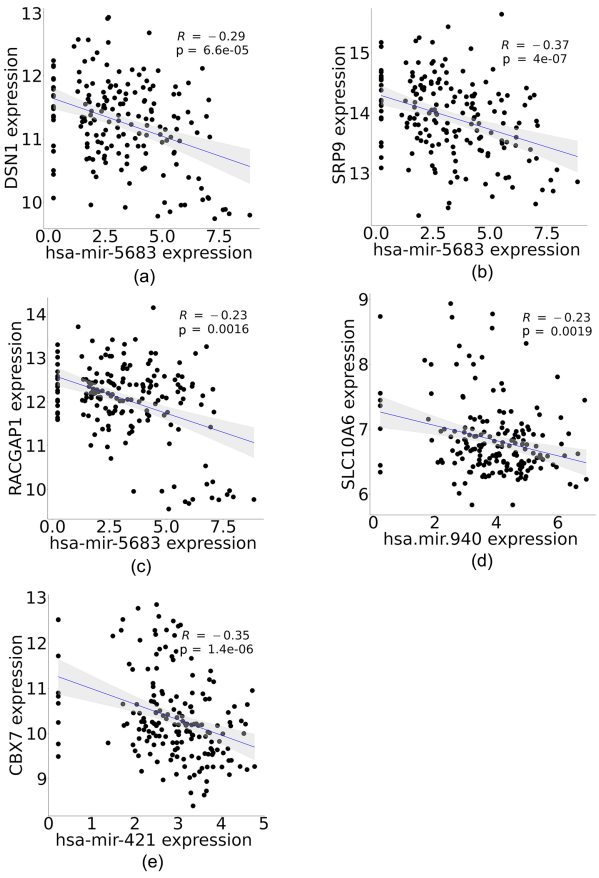


Figure 6. Spearman's correlation analysis of miRNA-target gene pairs in luminal B breast cancer patients. Scatter plots showing correlation between prognostic target genes ((a)-(d)) and miRNAs that target them, (a) DSN1, (b) SRP9, (c) RACGAP1, and (d) SLC10A6. (e) Scatter plot showing correlation between prognostic microRNA hsa-mir-421 with its target gene CBX7. X axis represents normalized expression values of miRNA; Y axis represents normalized expression values of mRNA. R is Spearman's correlation coefficient.

4. Discussion

Post-transcriptional regulation involves the binding of mature miRNAs mainly with the 3'UTR of target mRNAs at miRNA binding regions, resulting in the inhibition of translation or degradation of the transcript [17]. One miRNA is capable of targeting many genes, and multiple miRNAs can target the same gene [18]. Identifying the correct miRNA-mRNA pairs is necessary to understand the role of post-transcriptional regulation in the pathophysiology of luminal B breast cancer. In breast cancer, dysregulation of miRNAs is observed. In this study, we profiled differentially expressed mRNAs and miRNAs in luminal B breast cancers using TCGA data and identified significantly negatively regulated miRNA-target gene pairs.

The target genes were enriched for important pathways like the Ras signaling pathway and the PI3K-Akt signaling pathway. The PI3K/Akt pathway regulates cell growth, proliferation, and the cell cycle, and its dysregulation is associated with various cancers, including luminal B breast cancer. Aberrant post-transcriptional

regulation by miRNA contributes to impairment of this pathway, promoting cancer and drug resistance in various cancers, including breast cancer [19]-[21].

Further, miRNAs and corresponding target genes were investigated for the association of gene expression with survival, thus, identifying five genes, including miR-421, DSN1, SRP9, RACGAP1, and SLC10A6, with prognostic significance.

In our study, miR-421 was predicted to target Chromobox protein 7 (CBX7), and over-expression of miR-421 was significantly correlated with low expression of CBX7. According to Wang *et al.*, the expression of miR-421 was found to be up-regulated in breast cancer tissues, and knockdown of miR-421 inhibited breast cancer cell proliferation, invasiveness, and migration [22]. Consistent with our findings, miR-421 was reported to directly target the 3'UTR of CBX7, leading to its downregulation in ovarian cancer cells [23]. Similarly, in gastric cancer, inhibition of miR-421 was found to correlate with upregulation of the CBX7 gene [24].

In this study, the genes DSN1, SRP9 and RACGAP1 were predicted to be targeted by hsa-mir-5683. DSN1, a kinetochore protein, is a subunit of MTS12 kinetochore complex. It is involved in kinetochore assembly, accurate spindle microtubule attachment, and segregation of chromosomes during mitosis [25] [26]. DSN1 was found to be overexpressed in breast cancer [27]. Overexpression of DSN1 was found to be oncogenic and acts as a driver in HER2 (human epidermal growth factor receptor 2) negative breast cancers [28]. SRP9 is a protein subunit of signal recognition particle (SRP) complex. SRP9, along with SRP14 (Signal Recognition Particle 14), is involved in pausing the elongation of secretory and membrane proteins, and the SRP complex then targets the nascent polypeptide to the endoplasmic reticulum, where the resumption of translation occurs [29]. The expression of SRP9 was found to be upregulated in breast cancer [30]. RACGAP1 was found to play a role in cytokinesis and cell proliferation [31]. In breast cancer cells, overexpression of RACGAP1 contributes to mitochondrial-induced metastasis [32]. Overall survival was found to be poor in breast cancer patients with high RACGAP1 expression [33].

SLC10A6, also called SOAT (sodium-dependent organic anion transporter), is involved in the transport of all sulfated steroid hormones, including estrone-3-sulfate (E1S), and plays a role in fertility and the regulation of lipid metabolism [34]. In our study, we have observed that lower expression of SLC10A6 in luminal B breast cancer was strongly correlated with a lower probability of overall survival.

Overall, this work has resulted in identification of differential expressed miRNAs and associated pathways in luminal B breast cancers. It also resulted in identification of critical miRNA-target gene pairs and five genes of prognostic value in luminal B breast cancers. Further experimental analysis of these results may lead to better understanding of miRNA based post-transcriptional regulation in luminal B breast cancers.

Author Contributions

KU was associated with Conceptualization, Data curation, Formal Analysis, Investigation, Methodology and writing original draft of the study. RRA was

associated with Formal Analysis. SRH was associated with Conceptualization, Project administration, Supervision and writing review & editing. All authors read and approved the final manuscript.

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Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Publicly available datasets were analyzed in this study. This data can be found through https://www.cancer.gov/ccg/research/genome-sequencing/tcga.

Conflicts of Interest

The authors declare no conflict of interest.

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Supplementary Materials

Table S1. Differentially expressed miRNAs in luminal B breast cancers when compared to paired normal samples (|logFC| ≥ 1; FDR < 0.05).

	baseMean	log2FoldChange	lfcSE	stat	p-value	padj
hsa-mir-486-1	402.09502	−5.5992831	0.4883122	−11.466605	1.94E−30	2.53E−28
hsa-mir-486-2	400.72936	−5.5963788	0.4931908	−11.347288	7.65E−30	8.56E−28
hsa-mir-4732	1.678313	−4.3656044	0.8544777	−5.1090911	3.24E−07	2.15E−06
hsa-mir-451a	1471.0801	−4.3519348	0.4736035	−9.1889838	3.97E−20	1.48E−18
hsa-mir-204	9.1679416	−4.3184841	0.4911169	−8.793189	1.45E−18	4.38E−17
hsa-mir-144	289.3198	−4.1317836	0.4001404	−10.325834	5.38E−25	3.01E−23
hsa-mir-139	178.06392	−3.4733478	0.2674525	−12.986786	1.45E−38	5.69E−36
hsa-mir-6507	0.36804	−3.3320522	0.934781	−3.564527	0.0003645	0.0012973
hsa-mir-5683	24.479438	−3.1356124	0.5105627	−6.1414837	8.18E−10	9.02E−09
hsa-mir-1258	3.7869247	−3.1064665	0.4651514	−6.6783994	2.42E−11	3.10E−10
hsa-mir-452	83.951499	−3.0661116	0.3200866	−9.5790076	9.80E−22	4.04E−20
hsa-mir-6499	0.2518401	−2.9955008	1.2792924	−2.3415294	0.0192049	0.0444895
hsa-mir-133b	1.0426853	−2.9345684	0.8467618	−3.4656364	0.000529	0.0018235
hsa-mir-6715a	0.8742895	−2.9269317	0.6853255	−4.2708636	1.95E−05	9.71E−05
hsa-mir-99a	1571.1035	−2.9236587	0.2716027	−10.764467	5.07E−27	3.61E−25
hsa-mir-145	4531.6336	−2.9218705	0.2174404	−13.437569	3.64E−41	2.85E−38
hsa-mir-125b-1	895.36333	−2.7080958	0.2410073	−11.236571	2.70E−29	2.35E−27
hsa-mir-125b-2	924.39469	−2.6946571	0.2386078	−11.293248	1.42E−29	1.39E−27
hsa-mir-337	95.814563	−2.6741037	0.2609667	−10.246915	1.22E−24	6.38E−23
hsa-let-7c	4563.8277	−2.6657936	0.2523765	−10.562765	4.43E−26	2.67E−24
hsa-mir-934	1.0848851	−2.6376624	0.6582157	−4.007292	6.14E−05	0.0002672
hsa-mir-511	22.988378	−2.6195397	0.31138	−8.4126788	4.01E−17	1.01E−15
hsa-mir-100	6770.8633	−2.5006717	0.2476823	−10.096287	5.74E−24	2.64E−22
hsa-mir-665	1.153046	−2.4735475	0.3456823	−7.1555522	8.33E−13	1.28E−11
hsa-mir-205	5452.1479	−2.4533337	0.5098277	−4.8120836	1.49E−06	8.60E−06
hsa-mir-607	0.9443823	−2.4485692	0.4933442	−4.9632068	6.93E−07	4.27E−06
hsa-mir-483	13.180753	−2.4249812	0.3313186	−7.3191827	2.49E−13	4.25E−12
hsa-mir-133a-2	7.5623179	−2.4024777	0.5595407	−4.2936603	1.76E−05	8.94E−05
hsa-mir-585	1.5288913	−2.3990911	0.44057	−5.4454259	5.17E−08	3.71E−07

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hsa-mir-133a-1	8.3418292	−2.3776798	0.5605568	−4.2416398	2.22E−05	0.0001086
hsa-mir-551b	4.2851515	−2.3749172	0.3318399	−7.1568157	8.26E−13	1.28E−11
hsa-mir-584	85.565416	−2.3228587	0.2671677	−8.6943829	3.49E−18	1.01E−16
hsa-mir-6746	0.2895719	−2.2400447	0.7770778	−2.8826515	0.0039434	0.0113793
hsa-mir-378d-1	0.3647113	−2.2391925	0.5538497	−4.0429604	5.28E−05	0.0002348
hsa-mir-378a	637.23703	−2.2252757	0.2017619	−11.029217	2.76E−28	2.16E−26
hsa-mir-6513	0.3329167	−2.2215997	0.6615388	−3.3582307	0.0007844	0.0025807
hsa-mir-10b	221264.84	−2.2010546	0.2783316	−7.9080303	2.61E−15	5.12E−14
hsa-mir-1247	97.391629	−2.097876	0.4527959	−4.6331608	3.60E−06	1.97E−05
hsa-mir-378d-2	0.4306209	−2.0770332	0.5294013	−3.9233622	8.73E−05	0.0003716
hsa-mir-3199-1	0.7402999	−2.0500343	0.4003676	−5.1203803	3.05E−07	2.06E−06
hsa-mir-329-2	0.9684998	−2.0487001	0.3626569	−5.6491416	1.61E−08	1.34E−07
hsa-mir-378c	9.4502551	−2.046353	0.2267849	−9.023321	1.82E−19	6.21E−18
hsa-mir-224	69.355501	−2.0320418	0.4588992	−4.4280785	9.51E−06	5.06E−05
hsa-mir-329-1	0.6884448	−2.00735	0.4266703	−4.7046867	2.54E−06	1.43E−05
hsa-mir-7976	0.3503034	−2.0043497	0.6566987	−3.0521603	0.002272	0.006816
hsa-mir-3199-2	1.8436855	−1.9620287	0.2838771	−6.9115429	4.79E−12	6.95E−11
hsa-mir-6820	1.2918154	−1.9400861	0.3469019	−5.5926069	2.24E−08	1.79E−07
hsa-mir-4524a	0.3692785	−1.9289392	0.6824392	−2.8265362	0.0047054	0.0133009
hsa-mir-129-2	3.0914926	−1.925563	0.4468628	−4.30907	1.64E−05	8.39E−05
hsa-mir-495	15.76173	−1.9158719	0.212708	−9.0070513	2.12E−19	6.91E−18
hsa-mir-223	221.99261	−1.863759	0.2227777	−8.3660028	5.96E−17	1.46E−15
hsa-mir-140	1336.9093	−1.8556488	0.1535445	−12.085418	1.26E−33	2.47E−31
hsa-mir-6510	11.664277	−1.8492038	0.668622	−2.7656939	0.0056802	0.0156605
hsa-mir-433	2.4542096	−1.8293461	0.2649465	−6.9045865	5.03E−12	7.17E−11
hsa-mir-494	3.5821229	−1.8089136	0.2917317	−6.2006072	5.62E−10	6.29E−09
hsa-mir-376a-2	0.8098465	−1.8043181	0.4444626	−4.0595499	4.92E−05	0.0002225
hsa-mir-6720	0.7139041	−1.7782397	0.460535	−3.8612477	0.0001128	0.0004674
hsa-mir-432	11.798501	−1.7416987	0.2257058	−7.7166783	1.19E−14	2.12E−13
hsa-mir-1-1	6.8951249	−1.7410601	0.4923356	−3.536328	0.0004057	0.001431
hsa-mir-377	6.4125792	−1.7010712	0.2191166	−7.7633168	8.27E−15	1.51E−13
hsa-mir-1-2	7.744016	−1.6985119	0.4643349	−3.6579461	0.0002542	0.0009608

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hsa-mir-335	277.84375	−1.6910593	0.2477821	−6.8247843	8.81E−12	1.21E−10
hsa-mir-944	2.277033	−1.684255	0.4457249	−3.7786872	0.0001577	0.0006235
hsa-mir-1262	1.3944442	−1.6426683	0.4491916	−3.6569433	0.0002552	0.0009608
hsa-mir-195	108.92029	−1.6165908	0.2033469	−7.9499176	1.87E−15	3.75E−14
hsa-mir-381	50.375039	−1.5681606	0.211392	−7.4182575	1.19E−13	2.06E−12
hsa-mir-365b	322.83769	−1.5668955	0.1951496	−8.0292026	9.81E−16	2.08E−14
hsa-mir-6892	8.2133205	−1.5639456	0.28462	−5.4948543	3.91E−08	2.94E−07
hsa-mir-365a	324.7972	−1.5558726	0.1953663	−7.9638746	1.67E−15	3.44E−14
hsa-mir-4491	0.6484421	−1.5528886	0.6117487	−2.5384419	0.0111347	0.0273307
hsa-mir-299	6.6797129	−1.5505203	0.2543703	−6.0955249	1.09E−09	1.17E−08
hsa-mir-654	40.960674	−1.5363505	0.2203801	−6.9713678	3.14E−12	4.64E−11
hsa-mir-1295a	1.9631271	−1.4952316	0.3939937	−3.7950653	0.0001476	0.0005867
hsa-mir-379	1359.208	−1.4917966	0.2376766	−6.2765824	3.46E−10	4.04E−09
hsa-mir-3926-1	1.4021725	−1.4763144	0.3522423	−4.1911901	2.77E−05	0.0001309
hsa-mir-218-2	38.739212	−1.4431992	0.1735151	−8.3174274	8.99E−17	2.13E−15
hsa-mir-376c	9.5934551	−1.4387935	0.2358669	−6.1000225	1.06E−09	1.15E−08
hsa-mir-497	70.687982	−1.4345677	0.2270825	−6.3173858	2.66E−10	3.16E−09
hsa-mir-6716	2.0471718	−1.4304212	0.2688288	−5.3209367	1.03E−07	7.22E−07
hsa-mir-758	35.176244	−1.4237498	0.2546949	−5.5900208	2.27E−08	1.79E−07
hsa-mir-143	85641.998	−1.407558	0.2459538	−5.7228546	1.05E−08	9.43E−08
hsa-mir-218-1	40.290029	−1.401627	0.1779843	−7.8750034	3.41E−15	6.51E−14
hsa-mir-675	109.78128	−1.3851782	0.3604845	−3.8425453	0.0001218	0.0004966
hsa-mir-656	1.4412364	−1.3631296	0.390629	−3.4895761	0.0004838	0.0016761
hsa-mir-605	1.4451132	−1.3605147	0.4634516	−2.9356135	0.0033289	0.0097507
hsa-mir-485	8.9037422	−1.3595666	0.2406802	−5.6488506	1.62E−08	1.34E−07
hsa-mir-1468	14.817091	−1.3586537	0.3356995	−4.0472323	5.18E−05	0.0002319
hsa-mir-487b	9.9815635	−1.357503	0.2318963	−5.8539232	4.80E−09	4.76E−08
hsa-mir-129-1	2.6944645	−1.3161205	0.462013	−2.8486655	0.0043903	0.0125004
hsa-mir-3926-2	1.8357309	−1.3086125	0.3510385	−3.7278314	0.0001931	0.0007486
hsa-mir-326	36.906898	−1.3060986	0.3624045	−3.6039806	0.0003134	0.001136
hsa-mir-487a	2.7984448	−1.2933369	0.2777136	−4.6570885	3.21E−06	1.77E−05
hsa-mir-6803	0.5734836	−1.2932686	0.4626084	−2.7956013	0.0051803	0.0143967
hsa-mir-655	4.7897022	−1.2876925	0.2874926	−4.4790455	7.50E−06	4.02E−05
hsa-mir-190a	9.8607254	−1.2817773	0.2342274	−5.4723621	4.44E−08	3.25E−07

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hsa-mir-411	11.03217	−1.278277	0.2303751	−5.5486761	2.88E−08	2.23E−07
hsa-mir-6802	1.4582584	−1.2751502	0.2982265	−4.2757777	1.90E−05	9.56E−05
hsa-mir-676	1.9718384	−1.2675675	0.3209776	−3.9490843	7.85E−05	0.0003394
hsa-mir-130a	175.25575	−1.2471321	0.2388364	−5.2217001	1.77E−07	1.23E−06
hsa-mir-154	14.672667	−1.1965624	0.2135484	−5.603238	2.10E−08	1.70E−07
hsa-mir-126	9214.6322	−1.1915089	0.205058	−5.8105957	6.23E−09	5.94E−08
hsa-mir-29a	9057.9605	−1.158914	0.1727306	−6.7093741	1.95E−11	2.59E−10
hsa-mir-431	22.95481	−1.141606	0.2441096	−4.6766116	2.92E−06	1.62E−05
hsa-mir-3157	0.8226011	−1.1393032	0.412737	−2.7603611	0.0057738	0.0157521
hsa-mir-550a-3	3.64957	−1.138771	0.3600684	−3.1626517	0.0015634	0.0048194
hsa-mir-376b	3.0911758	−1.126789	0.3134812	−3.5944385	0.0003251	0.0011623
hsa-mir-320c-1	1.1200069	−1.113048	0.4145657	−2.684853	0.0072562	0.0187697
hsa-mir-6503	0.8519098	−1.0985206	0.4337047	−2.5328769	0.0113131	0.0276817
hsa-mir-1228	3.2982382	−1.0891062	0.2695065	−4.0411127	5.32E−05	0.000235
hsa-mir-323a	8.1561404	−1.0654165	0.2579785	−4.1298653	3.63E−05	0.0001672
hsa-mir-376a-1	2.6338564	−1.0630068	0.3199134	−3.3227957	0.0008912	0.0029075
hsa-mir-1271	8.4607772	−1.0519377	0.2603706	−4.0401561	5.34E−05	0.000235
hsa-mir-5187	0.8577444	−1.0433276	0.3862216	−2.7013705	0.0069054	0.0179633
hsa-mir-574	263.03563	−1.0290342	0.1914664	−5.3744893	7.68E−08	5.47E−07
hsa-mir-193a	1275.3023	−1.0129813	0.2003742	−5.0554488	4.29E−07	2.73E−06
hsa-mir-5010	1.8422211	−1.0126616	0.3145516	−3.2193815	0.0012847	0.004056
hsa-mir-369	18.336588	−1.0089761	0.2089231	−4.8294147	1.37E−06	8.06E−06
hsa-mir-4746	8.5648571	1.0014182	0.3422699	2.9258146	0.0034356	0.0099631
hsa-mir-15b	781.52829	1.0136852	0.2807298	3.6108926	0.0003051	0.0011165
hsa-mir-3678	2.4604492	1.0315012	0.4303483	2.3968982	0.0165345	0.0392319
hsa-mir-181b-2	417.77498	1.0532627	0.2625167	4.0121738	6.02E−05	0.0002632
hsa-mir-128-2	125.36257	1.0799044	0.2019114	5.3484082	8.87E−08	6.26E−07
hsa-mir-153-2	94.401054	1.0930262	0.3971377	2.7522604	0.0059185	0.0159801
hsa-mir-3917	3.2664687	1.1088028	0.4067737	2.7258465	0.0064137	0.0170234
hsa-mir-340	66.948502	1.1232094	0.1873446	5.9954198	2.03E−09	2.15E−08
hsa-mir-3200	15.729962	1.1397358	0.3500437	3.2559816	0.00113	0.0036262
hsa-mir-3928	6.7152949	1.1475131	0.3404641	3.3704383	0.0007505	0.00249
hsa-mir-671	23.29653	1.1692315	0.1987674	5.8824113	4.04E−09	4.11E−08
hsa-mir-130b	70.490573	1.2067833	0.206822	5.8348875	5.38E−09	5.27E−08

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hsa-mir-181b-1	486.95576	1.2155052	0.2589523	4.6939349	2.68E−06	1.50E−05
hsa-mir-548e	1.4325244	1.2284337	0.5098814	2.4092538	0.0159852	0.0380438
hsa-mir-628	111.94896	1.2382649	0.2539657	4.8757173	1.08E−06	6.43E−06
hsa-mir-149	636.8323	1.2391683	0.3244591	3.8191818	0.0001339	0.0005432
hsa-mir-659	3.8297918	1.2513507	0.3177915	3.9376462	8.23E−05	0.000354
hsa-mir-493	26.163156	1.2575993	0.2451146	5.1306574	2.89E−07	1.97E−06
hsa-mir-4677	26.158883	1.2594943	0.2014037	6.2535813	4.01E−10	4.62E−09
hsa-mir-5003	1.7666079	1.2689819	0.5530758	2.2944085	0.021767	0.0497125
hsa-mir-1180	37.177841	1.2749449	0.3473661	3.6703202	0.0002422	0.0009208
hsa-mir-92b	374.88802	1.2762793	0.3050507	4.1838261	2.87E−05	0.0001344
hsa-mir-3190	1.3821664	1.2775048	0.5530873	2.3097706	0.0209009	0.0479923
hsa-mir-32	68.37118	1.2864935	0.2194329	5.8628101	4.55E−09	4.57E−08
hsa-mir-191	3600.9051	1.294533	0.2288373	5.6570012	1.54E−08	1.31E−07
hsa-mir-345	78.85085	1.2954632	0.2947004	4.3958653	1.10E−05	5.84E−05
hsa-mir-7-1	116.64772	1.2994342	0.2548949	5.0979209	3.43E−07	2.26E−06
hsa-mir-421	6.821849	1.3280115	0.3148889	4.217397	2.47E−05	0.000118
hsa-mir-651	6.5527581	1.3336776	0.3272334	4.0756155	4.59E−05	0.0002089
hsa-mir-887	41.324838	1.3572844	0.3483161	3.8967027	9.75E−05	0.0004083
hsa-mir-3150b	8.1362897	1.3596496	0.4644834	2.9272299	0.00342	0.0099548
hsa-mir-1307	4081.0067	1.37424	0.2373037	5.7910599	6.99E−09	6.52E−08
hsa-mir-142	6877.4725	1.3894628	0.2782906	4.9928481	5.95E−07	3.70E−06
hsa-mir-1254-2	1.5203154	1.400673	0.5342434	2.6217884	0.008747	0.0220221
hsa-mir-3940	3.442979	1.4236549	0.4298656	3.3118608	0.0009268	0.0030111
hsa-mir-6777	1.9191851	1.4297281	0.5364216	2.6653068	0.0076918	0.0197581
hsa-mir-188	7.2544601	1.4403146	0.3308722	4.353084	1.34E−05	6.91E−05
hsa-mir-454	40.813627	1.4518643	0.2506854	5.7915788	6.97E−09	6.52E−08
hsa-mir-4728	12.1208	1.4555583	0.4959617	2.9348198	0.0033374	0.0097507
hsa-mir-3655	0.6146392	1.4641832	0.6014032	2.4346114	0.0149078	0.0359163
hsa-mir-1254-1	1.5347473	1.4684048	0.5327166	2.7564467	0.0058433	0.0158865
hsa-mir-4726	0.9534172	1.5212695	0.5962119	2.5515585	0.0107242	0.0264059
hsa-mir-4791	1.172677	1.5300713	0.5500166	2.781864	0.0054048	0.0149538
hsa-mir-2277	3.4943187	1.5483148	0.4120611	3.7574882	0.0001716	0.0006686
hsa-mir-200b	1624.7809	1.5567247	0.2461301	6.324805	2.54E−10	3.05E−09
hsa-mir-192	1469.6734	1.5589765	0.2754402	5.6599454	1.51E−08	1.30E−07

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hsa-mir-508	28.949204	1.5610572	0.4748114	3.2877419	0.0010099	0.0032677
hsa-mir-342	1466.4074	1.5717775	0.2862268	5.4913712	3.99E−08	2.97E−07
hsa-mir-3150a	0.6304385	1.5876974	0.612987	2.5900995	0.0095948	0.0240024
hsa-mir-3174	0.7027517	1.5948961	0.5999618	2.6583295	0.0078529	0.0200259
hsa-mir-3117	1.1553233	1.6004333	0.5810469	2.7543963	0.0058801	0.0159311
hsa-mir-1284	1.1407519	1.6009184	0.5825224	2.7482522	0.0059914	0.0161212
hsa-mir-5695	1.1546705	1.6039895	0.6036203	2.657282	0.0078774	0.0200259
hsa-mir-200c	29060.541	1.617704	0.1885213	8.581013	9.40E−18	2.54E−16
hsa-mir-4443	0.8817248	1.6299798	0.6353229	2.5655928	0.0103	0.0255218
hsa-mir-33a	55.270662	1.6390064	0.292117	5.6107876	2.01E−08	1.64E−07
hsa-mir-1537	0.737654	1.6422797	0.6183568	2.655877	0.0079102	0.0200444
hsa-mir-1276	0.5150502	1.6464775	0.6384312	2.5789427	0.0099103	0.0247127
hsa-mir-3127	31.568717	1.6518007	0.2840036	5.8161264	6.02E−09	5.82E−08
hsa-mir-514a-1	2.3547124	1.6613531	0.673698	2.4660205	0.0136624	0.0331196
hsa-mir-4442	0.7940265	1.6760927	0.6431355	2.606127	0.0091572	0.0229812
hsa-mir-639	1.5173041	1.6763994	0.5413423	3.0967457	0.0019566	0.005938
hsa-mir-615	49.520772	1.6875565	0.3766197	4.4807974	7.44E−06	4.02E−05
hsa-mir-148b	649.33419	1.6944818	0.197679	8.571885	1.02E−17	2.66E−16
hsa-mir-935	20.572243	1.7164173	0.6140348	2.7953093	0.005185	0.0143967
hsa-mir-3652	2.092463	1.7301788	0.5108944	3.3865681	0.0007077	0.0023581
hsa-mir-877	5.973361	1.7309915	0.4094693	4.2274021	2.36E−05	0.0001143
hsa-mir-4444-2	1.8782265	1.7385126	0.4923853	3.5307968	0.0004143	0.0014547
hsa-mir-6501	1.4267307	1.7843693	0.6804444	2.6223587	0.0087323	0.0220221
hsa-mir-4784	1.5369185	1.7963029	0.5582256	3.2178799	0.0012914	0.004061
hsa-mir-6798	1.1108443	1.8032359	0.6378251	2.8271634	0.0046962	0.0133009
hsa-mir-7-2	4.0426703	1.8116381	0.6038145	3.0003223	0.0026969	0.0080293
hsa-mir-4638	4.7189462	1.8132807	0.4132728	4.3876114	1.15E−05	5.98E−05
hsa-mir-940	19.49345	1.8282389	0.3549739	5.1503467	2.60E−07	1.79E−06
hsa-mir-203a	12496.575	1.9009597	0.3747564	5.0725203	3.93E−07	2.54E−06
hsa-mir-7974	0.8034344	1.9009722	0.7132812	2.6651092	0.0076963	0.0197581
hsa-mir-1224	6.1559971	1.9335091	0.6300641	3.0687501	0.0021496	0.0064735
hsa-mir-3690-1	1.4211261	1.9383949	0.6110464	3.1722547	0.0015126	0.0046999
hsa-mir-1301	49.23123	1.9419054	0.2483454	7.8193743	5.31E−15	9.90E−14
hsa-mir-9-2	1710.1567	1.9566892	0.5205485	3.7588986	0.0001707	0.0006681

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hsa-mir-3609	1.2756874	1.9580325	0.8544799	2.2914904	0.0219351	0.0499278
hsa-mir-9-1	1711.192	1.9811668	0.5200133	3.8098385	0.0001391	0.0005555
hsa-mir-9-3	1723.3757	1.9869663	0.5206257	3.8164967	0.0001354	0.0005439
hsa-mir-4326	25.497004	2.0001833	0.4147482	4.8226448	1.42E−06	8.28E−06
hsa-mir-5684	2.0404031	2.0244386	0.5168539	3.916849	8.97E−05	0.0003797
hsa-mir-4668	17.931526	2.0586947	0.3721219	5.5323122	3.16E−08	2.43E−07
hsa-mir-556	2.2265754	2.0593368	0.6172007	3.3365758	0.0008482	0.0027787
hsa-mir-7706	6.2067987	2.0762716	0.36429	5.6995027	1.20E−08	1.05E−07
hsa-mir-6854	2.3788626	2.0997995	0.4989254	4.2086439	2.57E−05	0.0001219
hsa-mir-3187	1.2252649	2.1157341	0.6166776	3.4308593	0.0006017	0.0020306
hsa-mir-1277	3.5964211	2.1287277	0.4348801	4.8949764	9.83E−07	5.92E−06
hsa-mir-301a	71.189087	2.1390784	0.3122654	6.850193	7.38E−12	1.03E−10
hsa-mir-3614	16.609324	2.1489317	0.4288585	5.010818	5.42E−07	3.40E−06
hsa-mir-4640	0.8494643	2.1540014	0.5933302	3.6303583	0.000283	0.0010546
hsa-mir-21	580260.95	2.1549576	0.2022222	10.656383	1.63E−26	1.06E−24
hsa-mir-4675	1.1349113	2.1599507	0.9101269	2.3732412	0.0176327	0.0412433
hsa-mir-200a	2259.243	2.1599869	0.2491628	8.6689784	4.36E−18	1.22E−16
hsa-mir-182	104572.93	2.200502	0.248791	8.8447807	9.17E−19	2.87E−17
hsa-mir-3619	1.6264388	2.2016167	0.5941509	3.705484	0.000211	0.0008108
hsa-mir-4714	2.4291421	2.2038305	0.7013232	3.1423893	0.0016758	0.0051254
hsa-mir-3176	0.81665	2.2041273	0.68999	3.1944337	0.0014011	0.0043881
hsa-mir-503	55.723256	2.2084052	0.3535234	6.2468427	4.19E−10	4.75E−09
hsa-mir-2114	2.5871486	2.2238264	0.6775979	3.2819263	0.001031	0.0033221
hsa-mir-4680	1.0308286	2.2777101	0.7185074	3.1700578	0.0015241	0.0047168
hsa-mir-3677	52.426063	2.2994318	0.3485839	6.5964942	4.21E−11	5.32E−10
hsa-mir-5694	3.4974724	2.3760376	0.6907293	3.4398967	0.0005819	0.0019725
hsa-mir-4758	0.9944876	2.376604	0.6430147	3.696034	0.000219	0.0008364
hsa-mir-1910	1.5046284	2.4076585	0.6498069	3.705191	0.0002112	0.0008108
hsa-mir-429	287.81234	2.4460055	0.2710352	9.0246777	1.80E−19	6.21E−18
hsa-mir-203b	136.27092	2.4541576	0.5605937	4.3777828	1.20E−05	6.22E−05
hsa-mir-187	63.910204	2.4625125	0.5773194	4.2654249	2.00E−05	9.89E−05
hsa-mir-141	4904.4781	2.4695679	0.2117873	11.660604	2.03E−31	3.17E−29
hsa-mir-3156-2	1.0068944	2.469967	1.0124368	2.4396258	0.0147025	0.035531
hsa-mir-3065	194.1868	2.6722265	0.466008	5.7342932	9.79E−09	9.02E−08

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hsa-mir-7156	2.9362456	2.6897926	0.8438436	3.1875486	0.0014348	0.004476
hsa-mir-3662	2.1014578	2.6983715	0.656894	4.1077734	3.99E−05	0.0001829
hsa-mir-4446	2.0919794	2.7451863	0.6566598	4.1805306	2.91E−05	0.0001355
hsa-mir-96	94.122746	2.8487537	0.2984195	9.5461382	1.35E−21	5.27E−20
hsa-mir-3664	3.0183011	2.925689	0.5991985	4.8826711	1.05E−06	6.26E−06
hsa-mir-4756	1.5154464	2.9370098	0.7484983	3.9238697	8.71E−05	0.0003716
hsa-mir-33b	27.096283	2.9473853	0.4101897	7.1854199	6.70E−13	1.07E−11
hsa-mir-301b	5.4643352	2.9940638	0.5238337	5.7156768	1.09E−08	9.72E−08
hsa-mir-760	14.67738	3.0452155	0.4764883	6.3909557	1.65E−10	2.02E−09
hsa-mir-3610	3.5277704	3.0726743	0.5606211	5.4808395	4.23E−08	3.13E−07
hsa-mir-183	45458.422	3.0857932	0.2409641	12.806028	1.52E−37	3.96E−35
hsa-mir-937	14.601024	3.0987091	0.520384	5.9546584	2.61E−09	2.69E−08
hsa-mir-4664	3.5072935	3.1943344	0.5846401	5.4637616	4.66E−08	3.38E−07
hsa-mir-7-3	4.0323959	3.2720805	0.6805728	4.807833	1.53E−06	8.72E−06
hsa-mir-375	69032.074	3.3010072	0.3985204	8.2831571	1.20E−16	2.76E−15
hsa-mir-210	2316.5797	3.3420528	0.329561	10.140924	3.64E−24	1.78E−22
hsa-mir-196a-2	1498.9541	3.4204973	0.479967	7.1265261	1.03E−12	1.55E−11
hsa-mir-7705	3.6540236	3.5305883	0.5393149	6.5464314	5.89E−11	7.32E−10
hsa-mir-4652	2.1866127	3.5469799	0.9294273	3.8163069	0.0001355	0.0005439
hsa-mir-190b	74.86657	3.5515278	0.3619959	9.8109614	1.01E−22	4.39E−21
hsa-mir-196a-1	1287.1559	3.5550906	0.4884056	7.2789722	3.36E−13	5.49E−12
hsa-mir-147b	3.4595148	3.8580574	0.6738046	5.7257808	1.03E−08	9.37E−08
hsa-mir-4501	5.3061953	3.8741146	0.7602908	5.0955696	3.48E−07	2.27E−06
hsa-mir-449c	3.5868192	4.0610001	1.1560968	3.5126817	0.0004436	0.0015506
hsa-mir-592	14.645961	4.1646147	0.5088097	8.185014	2.72E−16	5.92E−15
hsa-mir-184	98.86697	4.1782731	0.7004144	5.9654304	2.44E−09	2.55E−08
hsa-mir-1251	5.2776275	4.1854343	0.9762677	4.2871788	1.81E−05	9.14E−05
hsa-mir-767	12.299696	4.5122213	1.2908321	3.4955912	0.000473	0.0016461
hsa-mir-4724	8.4668685	4.7239329	0.6955226	6.7919184	1.11E−11	1.49E−10
hsa-mir-449b	8.2158557	4.894992	0.9674178	5.0598531	4.20E−07	2.69E−06
hsa-mir-105-2	22.126731	5.666011	1.2381268	4.5762768	4.73E−06	2.57E−05
hsa-mir-105-1	22.393353	5.785696	1.132057	5.1107816	3.21E−07	2.15E−06
hsa-mir-1269b	11.678364	5.7910783	1.319335	4.3893917	1.14E−05	5.97E−05
hsa-mir-449a	23.345357	6.6957718	0.9186087	7.2890362	3.12E−13	5.20E−12
hsa-mir-1269a	201.18322	8.4834144	1.0283411	8.2496114	1.59E−16	3.56E−15

Table S2. Critical miRNA-target gene pairs identified by spearman's correlation analysis (R < −0.2 and p-value < 0.05).

miRNA	miRNA-expression	Gene	Gene-expression	Spearman's_correlation_coefficient (R)	p-value
hsa-mir-5683	down	SRP9	up	−0.3672128	3.97E−07
hsa-mir-665	down	PDCL3	up	−0.3642548	4.99E−07
hsa-mir-665	down	SPC24	up	−0.3608442	6.49E−07
hsa-mir-944	down	YWHAZ	up	−0.3440701	2.25E−06
hsa-mir-665	down	CALR	up	−0.3372896	3.66E−06
hsa-mir-665	down	SLC25A22	up	−0.3348415	4.34E−06
hsa-mir-5683	down	KIF21A	up	−0.3345275	4.44E−06
hsa-mir-665	down	SNRNP25	up	−0.3342616	4.52E−06
hsa-mir-665	down	CENPM	up	−0.3267832	7.56E−06
hsa-mir-5683	down	MTFR1	up	−0.3191654	1.26E−05
hsa-mir-934	down	PMAIP1	up	−0.3181198	1.35E−05
hsa-mir-665	down	NR2F6	up	−0.3124445	1.95E−05
hsa-mir-665	down	NACC1	up	−0.3033006	3.49E−05
hsa-mir-665	down	EIF4A3	up	−0.3022335	3.73E−05
hsa-mir-665	down	BCAS4	up	−0.3021408	3.75E−05
hsa-mir-665	down	PGAM5	up	−0.2998268	4.33E−05
hsa-mir-665	down	SYNGR2	up	−0.2995249	4.41E−05
hsa-mir-5683	down	CCNB1	up	−0.2957081	5.57E−05
hsa-mir-1258	down	PACSIN1	up	−0.2951285	5.77E−05
hsa-mir-665	down	NECAB3	up	−0.2947845	5.89E−05
hsa-mir-5683	down	DSN1	up	−0.2930242	6.55E−05
hsa-mir-665	down	TPM3	up	−0.2903635	7.69E−05
hsa-mir-665	down	SYAP1	up	−0.2864156	9.70E−05
hsa-mir-665	down	ZNF695	up	−0.281877	0.0001264
hsa-mir-665	down	HJURP	up	−0.2817984	0.0001269
hsa-mir-665	down	PTRH2	up	−0.2801275	0.0001397
hsa-mir-665	down	PSMC4	up	−0.2757109	0.0001796
hsa-mir-1258	down	ZNF281	up	−0.2698214	0.0002493
hsa-mir-934	down	ASB16	up	−0.2669101	0.0002924
hsa-mir-5683	down	GPR141	up	−0.2630908	0.0003594
hsa-mir-5683	down	MORF4L2	up	−0.2569629	0.0004974
hsa-mir-5683	down	POLQ	up	−0.2568022	0.0005016
hsa-mir-665	down	CENPN	up	−0.2508178	0.0006836

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hsa-mir-665	down	RFC2	up	−0.2506172	0.0006906
hsa-mir-1262	down	CERS2	up	−0.2498418	0.0007185
hsa-mir-1262	down	AGMAT	up	−0.2425888	0.001034
hsa-mir-665	down	RRM2	up	−0.2414188	0.001095
hsa-mir-944	down	TSPAN13	up	−0.2407357	0.001133
hsa-mir-326	down	MAz	up	−0.2353943	0.001468
hsa-mir-665	down	GNG3	up	−0.2352009	0.001482
hsa-mir-5683	down	RACGAP1	up	−0.2330957	0.001638
hsa-mir-665	down	PRIM1	up	−0.2311795	0.001794
hsa-mir-665	down	RAD21	up	−0.2304525	0.001856
hsa-mir-665	down	TCEA3	up	−0.2293112	0.001958
hsa-mir-378c	down	DCTPP1	up	−0.2271472	0.002166
hsa-mir-5683	down	MTHFD2	up	−0.2251345	0.002377
hsa-mir-5683	down	PMAIP1	up	−0.2246175	0.002434
hsa-mir-665	down	DNA2	up	−0.2218089	0.002767
hsa-mir-665	down	AP1S3	up	−0.220575	0.002926
hsa-mir-665	down	BPNT1	up	−0.2185803	0.0032
hsa-mir-451a	down	HELLS	up	−0.2172289	0.00346
hsa-mir-665	down	BRI3BP	up	−0.2150804	0.003737
hsa-mir-326	down	RBM47	up	−0.2143822	0.003854
hsa-mir-1262	down	PTK6	up	−0.2137454	0.003963
hsa-mir-934	down	SERPINC1	up	−0.211244	0.004419
hsa-mir-665	down	ZNF623	up	−0.2062482	0.005473
hsa-mir-665	down	MRPL12	up	−0.2061883	0.005487
hsa-mir-326	down	PKM	up	−0.2058233	0.005573
hsa-mir-326	down	CD9	up	−0.203674	0.0061
hsa-mir-665	down	KCNK6	up	−0.2032562	0.006208
hsa-mir-429	up	QKI	down	−0.4347583	1.57E−09
hsa-mir-429	up	CDC14B	down	−0.4206447	5.82E−09
hsa-mir-375	up	EMP1	down	−0.4182187	7.23E−09
hsa-mir-190b	up	KLF6	down	−0.3900902	6.19E−08
hsa-mir-429	up	ACSL4	down	−0.3865243	1.07E−07
hsa-mir-429	up	ZEB2	down	−0.3733593	3.02E−07
hsa-mir-4501	up	ITGB8	down	−0.3670988	4.00E−07

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hsa-mir-429	up	ZFPM2	down	−0.3607663	7.82E−07
hsa-mir-190b	up	DAB2	down	−0.3544191	1.05E−06
hsa-mir-190b	up	GPC5	down	−0.3523811	1.23E−06
hsa-mir-375	up	KIT	down	−0.3522784	1.46E−06
hsa-mir-421	up	CBX7	down	−0.3509502	1.36E−06
hsa-mir-429	up	ANKRD33B	down	−0.3479079	1.99E−06
hsa-mir-429	up	TCF7L2	down	−0.3466486	2.18E−06
hsa-mir-3662	up	MYOCD	down	−0.3430709	2.42E−06
hsa-mir-375	up	F3	down	−0.3416484	3.09E−06
hsa-mir-375	up	YAP1	down	−0.339243	3.66E−06
hsa-mir-375	up	MAP3K8	down	−0.3325843	5.77E−06
hsa-mir-429	up	IGF2	down	−0.3270286	8.37E−06
hsa-mir-429	up	TCF7L1	down	−0.3224606	1.13E−05
hsa-mir-190b	up	CYGB	down	−0.3167686	1.48E−05
hsa-mir-190b	up	IGF1	down	−0.3154332	1.61E−05
hsa-mir-4326	up	TXNIP	down	−0.3146926	1.69E−05
hsa-mir-375	up	ZFP36L2	down	−0.3126845	2.12E−05
hsa-mir-1269a	up	H6PD	down	−0.3117793	2.04E−05
hsa-mir-4784	up	HAP1	down	−0.3103257	2.24E−05
hsa-mir-940	up	PER2	down	−0.3036045	3.43E−05
hsa-mir-3652	up	PRKCA	down	−0.2999963	4.29E−05
hsa-mir-5694	up	ANTXR2	down	−0.2985284	4.69E−05
hsa-mir-375	up	CELF2	down	−0.293507	6.85E−05
hsa-mir-3662	up	PTPN14	down	−0.290054	7.83E−05
hsa-mir-375	up	TNS1	down	−0.2894266	8.70E−05
hsa-mir-375	up	SH3D19	down	−0.2888155	9.02E−05
hsa-miR-592	up	AKAP12	down	−0.2843705	0.0001094
hsa-mir-375	up	ACSL4	down	−0.2810766	0.0001405
hsa-mir-3609	up	ADAMTS9	down	−0.2807031	0.0001352
hsa-mir-429	up	AVPR1A	down	−0.2803296	0.0001465
hsa-mir-375	up	GATA6	down	−0.2760682	0.000186
hsa-mir-375	up	AKAP7	down	−0.2759715	0.000187
hsa-mir-429	up	KLF11	down	−0.2738521	0.0002102
hsa-mir-3652	up	SIK2	down	−0.2734481	0.0002039

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hsa-mir-4784	up	WFIKKN2	down	−0.2719226	0.0002219
hsa-mir-449a	up	MET	down	−0.2714277	0.0002281
hsa-miR-592	up	CCL16	down	−0.2659841	0.0003075
hsa-mir-3662	up	ETS2	down	−0.2650204	0.0003239
hsa-mir-190b	up	PCDHB11	down	−0.2645826	0.0003317
hsa-mir-940	up	NPR1	down	−0.2634869	0.0003519
hsa-mir-940	up	OLFML2A	down	−0.262919	0.0003628
hsa-mir-3652	up	ABCA6	down	−0.2615974	0.0003893
hsa-mir-429	up	JUN	down	−0.2612797	0.0004134
hsa-mir-375	up	FAM89A	down	−0.2570923	0.0005141
hsa-mir-3652	up	PTGIS	down	−0.2557748	0.0005292
hsa-mir-3662	up	SLC35G2	down	−0.2545139	0.0005651
hsa-mir-375	up	SAMD4A	down	−0.2495571	0.0007548
hsa-mir-4326	up	TNS1	down	−0.2495448	0.0007294
hsa-mir-449a	up	TXNIP	down	−0.2463247	0.0008583
hsa-mir-7705	up	CYGB	down	−0.245438	0.0008973
hsa-mir-940	up	CDC14B	down	−0.2446813	0.0009318
hsa-mir-7705	up	KLHL3	down	−0.2409715	0.00112
hsa-mir-940	up	EPHA2	down	−0.2385039	0.001263
hsa-mir-1276	up	ACVR2A	down	−0.2379292	0.001299
hsa-mir-3609	up	KLF6	down	−0.2375235	0.001325
hsa-mir-5695	up	CHST3	down	−0.2370087	0.001358
hsa-mir-429	up	WASF3	down	−0.2364764	0.001432
hsa-miR-1284	up	RCAN2	down	−0.2360124	0.001425
hsa-mir-190b	up	PM20D2	down	−0.2353593	0.00147
hsa-mir-7705	up	CYP27C1	down	−0.2335649	0.001602
hsa-mir-375	up	PIK3IP1	down	−0.2328055	0.001703
hsa-mir-940	up	TLN1	down	−0.2312545	0.001788
hsa-mir-940	up	FOXC1	down	−0.2311928	0.001793
hsa-mir-940	up	SLC10A6	down	−0.2299449	0.001901
hsa-mir-5695	up	BACH2	down	−0.2288609	0.002
hsa-mir-375	up	LDHB	down	−0.2283033	0.0021
hsa-mir-5695	up	SOX17	down	−0.2277192	0.002109
hsa-mir-375	up	SYT15	down	−0.2276243	0.002167

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hsa-mir-3662	up	ADAMTS1	down	−0.2240943	0.002493
hsa-mir-449a	up	FOXN3	down	−0.2239901	0.002505
hsa-mir-147b	up	MITF	down	−0.2232909	0.002587
hsa-mir-7705	up	LAMA4	down	−0.2226293	0.002666
hsa-mir-1269b	up	H6PD	down	−0.2213294	0.002828
hsa-mir-3652	up	MYH11	down	−0.2208941	0.002884
hsa-mir-3662	up	SH3TC2	down	−0.2203975	0.002949
hsa-mir-5695	up	SLC22A3	down	−0.2182073	0.003254
hsa-miR-592	up	EMCN	down	−0.2179502	0.003291
hsa-mir-449a	up	CLIC5	down	−0.2173743	0.003377
hsa-mir-449a	up	UST	down	−0.2173198	0.003385
hsa-mir-940	up	ADD2	down	−0.2168689	0.003453
hsa-mir-5695	up	ITGA9	down	−0.2160662	0.003578
hsa-mir-375	up	PRKCA	down	−0.2160478	0.003644
hsa-mir-3662	up	SEMA6D	down	−0.2141494	0.003893
hsa-mir-449a	up	NOTCH1	down	−0.2120725	0.004263
hsa-mir-4326	up	AMOTL1	down	−0.210992	0.004468
hsa-mir-3652	up	FBXO40	down	−0.2108282	0.004499
hsa-mir-3652	up	OMD	down	−0.2097977	0.004704
hsa-miR-1284	up	HOXA9	down	−0.2095338	0.004757
hsa-mir-1276	up	AKAP6	down	−0.2086087	0.00495
hsa-mir-3652	up	TSHZ2	down	−0.2082591	0.005025
hsa-mir-375	up	NCOA7	down	−0.2069097	0.005397
hsa-mir-940	up	PDE7B	down	−0.2058106	0.005576
hsa-mir-760	up	ETS1	down	−0.2053226	0.005692
hsa-mir-940	up	NPY4R	down	−0.2047089	0.005841
hsa-mir-3662	up	ACSL4	down	−0.2032589	0.006207
hsa-mir-5695	up	PDE1A	down	−0.2024794	0.006412
hsa-miR-592	up	EPHA4	down	−0.2005619	0.006943

Table S3. Differentially expressed target genes in luminal B breast cancer.

gene_id	gene_name	baseMean	log2FoldChange	lfcSE	stat	p-value	padj
ENSG00000133392.18	MYH11	4182.333	−4.73722	0.263733	−17.9622	3.85E−72	8.36E−70
ENSG00000169418.10	NPR1	994.8141	−4.40846	0.222879	−19.7796	4.46E−87	3.33E−84
ENSG00000157404.16	KIT	2759.348	−4.29016	0.382646	−11.2118	3.57E−29	1.05E−27

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ENSG00000204174.8	NPY4R	1.131372	−4.24808	0.666555	−6.37318	1.85E−10	1.21E−09
ENSG00000275152.5	CCL16	6.107794	−3.6132	0.39113	−9.23786	2.51E−20	4.17E−19
ENSG00000154262.13	ABCA6	526.0594	−3.59807	0.267015	−13.4752	2.19E−41	1.25E−39
ENSG00000163833.8	FBXO40	2.115284	−3.53501	0.49209	−7.18366	6.79E−13	5.80E−12
ENSG00000182463.16	TSHZ2	1015.632	−3.46184	0.221596	−15.6223	5.13E−55	5.70E−53
ENSG00000017427.17	IGF1	146.2573	−3.43134	0.305261	−11.2407	2.57E−29	7.61E−28
ENSG00000079308.19	TNS1	13105.78	−3.42972	0.158007	−21.7062	1.79E−104	4.19E−101
ENSG00000146477.6	SLC22A3	125.967	−3.30656	0.394025	−8.39175	4.79E−17	5.97E−16
ENSG00000131016.17	AKAP12	2643.414	−3.26625	0.236728	−13.7975	2.64E−43	1.66E−41
ENSG00000154734.16	ADAMTS1	3428.261	−3.26333	0.3076	−10.609	2.71E−26	6.63E−25
ENSG00000164736.6	SOX17	205.1572	−3.12087	0.203069	−15.3686	2.66E−53	2.71E−51
ENSG00000054598.9	FOXC1	425.2381	−3.03671	0.232089	−13.0843	4.05E−39	2.07E−37
ENSG00000141052.18	MYOCD	49.80311	−2.95209	0.423622	−6.9687	3.20E−12	2.53E−11
ENSG00000164035.10	EMCN	1083.569	−2.80775	0.193672	−14.4974	1.26E−47	9.43E−46
ENSG00000105976.16	MET	1435.458	−2.77559	0.357854	−7.7562	8.75E−15	8.92E−14
ENSG00000170145.5	SIK2	3313.581	−2.77356	0.176112	−15.7488	7.00E−56	8.43E−54
ENSG00000134531.10	EMP1	11291.44	−2.74574	0.208157	−13.1907	9.93E−40	5.19E−38
ENSG00000124212.6	PTGIS	1898.959	−2.72032	0.337166	−8.06819	7.13E−16	8.00E−15
ENSG00000117525.14	F3	1222.6	−2.71613	0.312218	−8.69948	3.33E−18	4.59E−17
ENSG00000182118.8	FAM89A	394.7037	−2.71104	0.402906	−6.72871	1.71E−11	1.26E−10
ENSG00000145283.8	SLC10A6	41.70076	−2.64108	0.323546	−8.16293	3.27E−16	3.78E−15
ENSG00000137872.17	SEMA6D	476.5353	−2.61329	0.323742	−8.07216	6.91E−16	7.76E−15
ENSG00000169247.14	SH3TC2	102.764	−2.60906	0.271145	−9.62237	6.43E−22	1.19E−20
ENSG00000048740.18	CELF2	2009.801	−2.54104	0.237201	−10.7126	8.88E−27	2.24E−25
ENSG00000168917.9	SLC35G2	212.4747	−2.53843	0.226704	−11.1971	4.21E−29	1.23E−27
ENSG00000081377.17	CDC14B	722.5051	−2.49492	0.224796	−11.0986	1.27E−28	3.59E−27
ENSG00000132970.14	WASF3	391.7932	−2.46931	0.347207	−7.11193	1.14E−12	9.54E−12
ENSG00000122863.6	CHST3	1141.86	−2.41879	0.222482	−10.8718	1.57E−27	4.14E−26
ENSG00000265972.6	TXNIP	41624.99	−2.40691	0.221344	−10.8741	1.53E−27	4.05E−26
ENSG00000152284.5	TCF7L1	1180.151	−2.40503	0.277114	−8.67886	4.00E−18	5.45E−17
ENSG00000152104.12	PTPN14	3239.542	−2.3832	0.202184	−11.7873	4.54E−32	1.56E−30
ENSG00000173805.16	HAP1	77.31086	−2.36633	0.469786	−5.03704	4.73E−07	1.94E−06
ENSG00000020577.14	SAMD4A	944.5597	−2.32662	0.218535	−10.6464	1.81E−26	4.49E−25
ENSG00000112782.19	CLIC5	483.722	−2.32626	0.304194	−7.6473	2.05E−14	2.03E−13

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ENSG00000204176.14	SYT15	21.12648	−2.30239	0.249285	−9.23597	2.56E−20	4.24E−19
ENSG00000112182.15	BACH2	257.1657	−2.26902	0.256459	−8.84749	8.95E−19	1.29E−17
ENSG00000177606.8	JUN	11479.81	−2.26689	0.228937	−9.90181	4.09E−23	8.22E−22
ENSG00000109686.19	SH3D19	4541.498	−2.24316	0.170627	−13.1466	1.78E−39	9.21E−38
ENSG00000171408.14	PDE7B	172.8577	−2.23779	0.204487	−10.9435	7.14E−28	1.93E−26
ENSG00000154229.12	PRKCA	429.3344	−2.17213	0.219209	−9.90898	3.81E−23	7.68E−22
ENSG00000163297.17	ANTXR2	2568.571	−2.17205	0.215654	−10.0719	7.35E−24	1.57E−22
ENSG00000142627.13	EPHA2	776.7399	−2.15179	0.190524	−11.2941	1.40E−29	4.21E−28
ENSG00000157557.13	ETS2	2737.954	−2.14215	0.169751	−12.6193	1.65E−36	7.13E−35
ENSG00000100307.13	CBX7	1545.103	−2.07287	0.209027	−9.91675	3.52E−23	7.15E−22
ENSG00000167244.21	IGF2	115.9528	−2.06731	0.319724	−6.46592	1.01E−10	6.80E−10
ENSG00000146281.6	PM20D2	570.7357	−2.05834	0.375368	−5.48351	4.17E−08	1.99E−07
ENSG00000166025.18	AMOTL1	2390.428	−2.04661	0.251772	−8.12879	4.34E−16	4.97E−15
ENSG00000163638.13	ADAMTS9	778.2113	−2.03456	0.186902	−10.8857	1.35E−27	3.59E−26
ENSG00000151320.11	AKAP6	264.7078	−2.01836	0.279149	−7.23039	4.82E−13	4.20E−12
ENSG00000161544.10	CYGB	603.7304	−2.01109	0.225797	−8.90663	5.26E−19	7.75E−18
ENSG00000111912.20	NCOA7	2513.176	−1.98953	0.209973	−9.47517	2.66E−21	4.71E−20
ENSG00000164236.12	ANKRD33B	267.3435	−1.95984	0.253401	−7.73414	1.04E−14	1.06E−13
ENSG00000144668.12	ITGA9	989.5649	−1.92159	0.213808	−8.98743	2.53E−19	3.83E−18
ENSG00000173714.8	WFIKKN2	5.471032	−1.91422	0.571935	−3.34692	0.000817	0.001955
ENSG00000169554.22	ZEB2	2546.417	−1.90165	0.199745	−9.52041	1.73E−21	3.09E−20
ENSG00000115252.18	PDE1A	234.1435	−1.89086	0.195606	−9.66667	4.18E−22	7.80E−21
ENSG00000152518.8	ZFP36L2	5244.958	−1.87946	0.223518	−8.40853	4.15E−17	5.21E−16
ENSG00000078399.19	HOXA9	138.6752	−1.87249	0.45164	−4.14598	3.38E−05	0.000104
ENSG00000053254.16	FOXN3	3115.684	−1.85297	0.175675	−10.5477	5.20E−26	1.26E−24
ENSG00000067082.15	KLF6	11675.17	−1.73614	0.171046	−10.1502	3.31E−24	7.22E−23
ENSG00000112769.20	LAMA4	6728.366	−1.72278	0.204349	−8.43058	3.44E−17	4.34E−16
ENSG00000148737.17	TCF7L2	1593.452	−1.70318	0.226376	−7.52366	5.33E−14	5.10E−13
ENSG00000111962.8	UST	607.7603	−1.68847	0.351058	−4.80965	1.51E−06	5.74E−06
ENSG00000172348.15	RCAN2	704.8905	−1.68334	0.185449	−9.0771	1.12E−19	1.74E−18
ENSG00000105855.10	ITGB8	1433.504	−1.66527	0.411121	−4.05055	5.11E−05	0.000152
ENSG00000127083.7	OMD	867.1152	−1.65735	0.412603	−4.01681	5.90E−05	0.000173
ENSG00000068366.20	ACSL4	2179.473	−1.65119	0.21483	−7.68603	1.52E−14	1.52E−13
ENSG00000107968.10	MAP3K8	790.9698	−1.62605	0.268341	−6.05964	1.36E−09	7.98E−09

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ENSG00000172059.11	KLF11	1572.929	−1.62369	0.154556	−10.5055	8.15E−26	1.95E−24
ENSG00000169946.14	ZFPM2	457.4484	−1.59802	0.267775	−5.96777	2.41E−09	1.36E−08
ENSG00000146021.15	KLHL3	442.0001	−1.566	0.256042	−6.11618	9.58E−10	5.73E−09
ENSG00000112531.17	QKI	5172.184	−1.56491	0.17405	−8.99115	2.45E−19	3.72E−18
ENSG00000179399.15	GPC5	6.517002	−1.56448	0.48903	−3.19915	0.001378	0.003163
ENSG00000166148.4	AVPR1A	512.6131	−1.52204	0.329728	−4.61604	3.91E−06	1.39E−05
ENSG00000187098.17	MITF	1058.335	−1.5204	0.239991	−6.33522	2.37E−10	1.53E−09
ENSG00000116106.12	EPHA4	743.7578	−1.48305	0.349354	−4.24512	2.18E−05	6.94E−05
ENSG00000075340.23	ADD2	227.8462	−1.45992	0.343043	−4.2558	2.08E−05	6.64E−05
ENSG00000132326.12	PER2	2618.643	−1.44958	0.144443	−10.0357	1.06E−23	2.24E−22
ENSG00000137693.14	YAP1	5476.509	−1.40184	0.199666	−7.02094	2.20E−12	1.77E−11
ENSG00000153071.15	DAB2	4863.07	−1.39153	0.207863	−6.69447	2.16E−11	1.58E−10
ENSG00000134954.14	ETS1	5635.614	−1.37916	0.191642	−7.19655	6.18E−13	5.31E−12
ENSG00000186684.14	CYP27C1	22.23172	−1.36	0.343668	−3.95732	7.58E−05	0.000218
ENSG00000197479.7	PCDHB11	122.8965	−1.33616	0.363511	−3.6757	0.000237	0.000626
ENSG00000049239.13	H6PD	5899.722	−1.30308	0.126274	−10.3195	5.76E−25	1.31E−23
ENSG00000185585.20	OLFML2A	3008.681	−1.29205	0.203804	−6.33965	2.30E−10	1.49E−09
ENSG00000141448.11	GATA6	252.49	−1.28394	0.247251	−5.19285	2.07E−07	8.96E−07
ENSG00000111716.14	LDHB	258.771	−1.25185	0.336054	−3.72514	0.000195	0.000525
ENSG00000148400.12	NOTCH1	2767.299	−1.21422	0.147763	−8.21738	2.08E−16	2.45E−15
ENSG00000100100.13	PIK3IP1	2570.633	−1.15021	0.157226	−7.31564	2.56E−13	2.31E−12
ENSG00000121989.15	ACVR2A	833.1735	−1.11146	0.176357	−6.30234	2.93E−10	1.87E−09
ENSG00000137076.21	TLN1	24040.19	−1.0122	0.142752	−7.09064	1.33E−12	1.11E−11
ENSG00000118507.17	AKAP7	442.2442	−1.00969	0.209109	−4.82852	1.38E−06	5.25E−06
ENSG00000067225.18	PKM	63589.19	1.003789	0.14141	7.098408	1.26E−12	1.05E−11
ENSG00000010278.15	CD9	27313.29	1.03073	0.174172	5.917889	3.26E−09	1.81E−08
ENSG00000162813.18	BPNT1	3818.101	1.032864	0.138539	7.455396	8.96E−14	8.46E−13
ENSG00000179218.14	CALR	47750.32	1.056944	0.159821	6.613301	3.76E−11	2.66E−10
ENSG00000162702.8	ZNF281	3935.303	1.056971	0.178739	5.913478	3.35E−09	1.85E−08
ENSG00000204219.11	TCEA3	4844.245	1.060776	0.194272	5.460249	4.75E−08	2.25E−07
ENSG00000013275.8	PSMC4	6371.815	1.073648	0.113419	9.466174	2.90E−21	5.11E−20
ENSG00000115539.14	PDCL3	1999.501	1.076507	0.122667	8.775874	1.70E−18	2.38E−17
ENSG00000163694.15	RBM47	10668.08	1.107651	0.148473	7.460285	8.63E−14	8.17E−13
ENSG00000143742.14	SRP9	17143.41	1.162208	0.147817	7.862505	3.77E−15	3.93E−14

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ENSG00000247077.7	PGAM5	3686.237	1.162817	0.123098	9.446263	3.51E−21	6.13E−20
ENSG00000049541.11	RFC2	2610.376	1.18846	0.128301	9.263053	1.99E−20	3.32E−19
ENSG00000152056.17	AP1S3	382.8773	1.188634	0.195606	6.076678	1.23E−09	7.23E−09
ENSG00000141543.12	EIF4A3	9157.783	1.193752	0.143133	8.34013	7.42E−17	9.08E−16
ENSG00000123562.18	MORF4L2	25317.37	1.220208	0.165276	7.382856	1.55E−13	1.43E−12
ENSG00000198056.15	PRIM1	516.0286	1.253897	0.163747	7.657537	1.90E−14	1.88E−13
ENSG00000183309.12	ZNF623	5290.028	1.258205	0.178412	7.052244	1.76E−12	1.44E−11
ENSG00000164924.18	YWHAZ	97012.07	1.308363	0.190907	6.853413	7.21E−12	5.51E−11
ENSG00000169895.6	SYAP1	12361.49	1.323317	0.190062	6.96254	3.34E−12	2.64E−11
ENSG00000141378.15	PTRH2	2313.839	1.344021	0.234938	5.720745	1.06E−08	5.49E−08
ENSG00000139116.19	KIF21A	2617.672	1.371612	0.182837	7.501817	6.29E−14	6.00E−13
ENSG00000117601.14	SERPINC1	14.6167	1.380024	0.344103	4.010498	6.06E−05	0.000178
ENSG00000143549.21	TPM3	35311.88	1.394759	0.115391	12.08724	1.23E−33	4.62E−32
ENSG00000179958.10	DCTPP1	3178.149	1.480657	0.169935	8.713072	2.96E−18	4.08E−17
ENSG00000066855.16	MTFR1	3421.341	1.490422	0.209157	7.125854	1.03E−12	8.67E−12
ENSG00000160113.5	NR2F6	4102.62	1.508661	0.190579	7.916191	2.45E−15	2.61E−14
ENSG00000164754.15	RAD21	35872.35	1.521572	0.199188	7.638873	2.19E−14	2.17E−13
ENSG00000143418.20	CERS2	13470.45	1.53076	0.167388	9.144967	5.96E−20	9.50E−19
ENSG00000160877.6	NACC1	5695.161	1.571444	0.160161	9.811627	1.00E−22	1.96E−21
ENSG00000108639.8	SYNGR2	21865.43	1.573168	0.222722	7.063368	1.63E−12	1.33E−11
ENSG00000166451.13	CENPN	525.2235	1.582459	0.165603	9.555762	1.23E−21	2.23E−20
ENSG00000103495.14	MAZ	1324.477	1.584558	0.153138	10.34727	4.31E−25	9.90E−24
ENSG00000149636.16	DSN1	2614.142	1.608786	0.148041	10.86716	1.65E−27	4.34E−26
ENSG00000116771.6	AGMAT	199.9316	1.623433	0.269733	6.018662	1.76E−09	1.01E−08
ENSG00000184992.13	BRI3BP	3135.055	1.627688	0.138192	11.77842	5.04E−32	1.72E−30
ENSG00000262814.8	MRPL12	266.1392	1.630506	0.356902	4.568502	4.91E−06	1.72E−05
ENSG00000177542.11	SLC25A22	2302.414	1.642046	0.18744	8.760402	1.95E−18	2.72E−17
ENSG00000187037.8	GPR141	79.99273	1.700932	0.380754	4.46727	7.92E−06	2.70E−05
ENSG00000099337.5	KCNK6	4163.652	1.716541	0.229608	7.475959	7.66E−14	7.28E−13
ENSG00000161664.7	ASB16	156.6078	1.727263	0.299618	5.764878	8.17E−09	4.31E−08
ENSG00000065911.13	MTHFD2	5783.556	1.727698	0.17727	9.746149	1.92E−22	3.67E−21
ENSG00000161981.11	SNRNP25	3015.774	1.782309	0.174774	10.1978	2.03E−24	4.47E−23
ENSG00000125967.17	NECAB3	3696.475	1.989247	0.23244	8.558109	1.15E−17	1.51E−16
ENSG00000141682.12	PMAIP1	1307.21	2.065221	0.314488	6.566933	5.14E−11	3.58E−10

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ENSG00000138346.15	DNA2	816.1066	2.106384	0.174439	12.07518	1.43E−33	5.34E−32
ENSG00000119969.15	HELLS	1568.739	2.154497	0.174916	12.31732	7.31E−35	2.89E−33
ENSG00000106537.8	TSPAN13	27275.54	2.184523	0.232017	9.415377	4.71E−21	8.18E−20
ENSG00000162188.6	GNG3	6.381731	2.274225	0.428108	5.312272	1.08E−07	4.87E−07
ENSG00000101213.7	PTK6	1491.814	2.443841	0.269593	9.064913	1.25E−19	1.93E−18
ENSG00000161800.13	RACGAP1	4784.994	2.580521	0.149218	17.29362	5.25E−67	8.61E−65
ENSG00000124243.17	BCAS4	2761.958	2.611711	0.240577	10.85604	1.87E−27	4.89E−26
ENSG00000134057.15	CCNB1	4642.506	3.105306	0.163561	18.98566	2.24E−80	9.30E−78
ENSG00000100162.15	CENPM	740.1221	3.221654	0.234838	13.71861	7.86E−43	4.76E−41
ENSG00000051341.14	POLQ	792.2459	3.224711	0.188866	17.07406	2.32E−65	3.66E−63
ENSG00000124507.11	PACSIN1	401.357	3.395711	0.328254	10.34476	4.42E−25	1.02E−23
ENSG00000161888.11	SPC24	910.7969	3.459886	0.198499	17.43026	4.86E−68	8.49E−66
ENSG00000197472.15	ZNF695	125.6736	3.480798	0.354153	9.828508	8.49E−23	1.66E−21
ENSG00000123485.12	HJURP	1205.887	4.037869	0.176764	22.8433	1.70E−115	7.95E−112
ENSG00000171848.16	RRM2	5165.332	4.254322	0.224536	18.94716	4.66E−80	1.85E−77