Genomic analyses identify biological processes of miR-125 mediated breast cancer cells

Hongmei Guo

Wei Zhang

Guangqi Liu

Tingxiang Chang

Hanming Gu (✉ laygmp@gmail.com)

Research Article

Keywords:

Posted Date: December 30th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-1214908/v1>

License: This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

miRNAs contain suppressive and oncogenic properties to regulate the progression of cancers. The expression of miR-125b is reported to be consistently low in breast cancers. However, the function and mechanism of miR-125b are not fully understood in breast cancers. In our study, our objective is to identify the DEGs and biological processes in the miR-125b mediated breast cancer cells by analyzing the RNA-seq data. The GSE123358 dataset was produced by the Illumina HiSeq 2000 (Homo sapiens). The KEGG and GO analyses showed the mitochondria and endoplasmic reticulum oxidative phosphorylation pathways are the main processes in miR-125b mediated breast cancer. Moreover, we identified ten interactive molecules including UQCRC1, CALR, HNRNPB, ATP5G1, NDUFB11, UQCRC1, HSP90B1, TGOLN2, SAP18, and XPOT. Thus, our study may benefit the treatment of breast cancer by using miR-125b.

Introduction

Breast cancer is a heterogeneous disease, which is the most common cancer in women¹. Recently, treatments have been involved in more biologically-directed therapies to decrease the adverse effects². Early breast cancer is considered curable due to the reason that cancer only spreads to the axillary lymph nodes³. Improvements in multiple therapies contribute to enhancing chances for cure in most patients⁴. Conversely, metastatic diseases are not curable by using the available therapeutic methods⁵. For metastatic cancer, the main goals of therapy are to prolong survival and improve quality of life⁶.

Small RNAs are defined by their length and association with AGO family proteins, which are divided into three classes including miRNA, siRNA, and piRNA⁷. miRNA contains about 22 nucleotides and are created by RNase III proteins, Drosha, and Dicer⁸. miRNA functions as a guide by matching its target mRNAs, whereas AGO proteins function as translational repressors and mRNA decay⁹. The miRNA regulation involves multiple steps such as transcription and Drosha/Dicer procession¹⁰. Most protein-coding genes include at least one conserved miRNA-binding site, which may be directly regulated by miRNAs¹¹.

miR-125 is an important mediator in cancers, which binds to the RNA-induced silencing complex (RISC) to degrade the target mRNAs or inhibit the translation through binding the 3'UTRs¹². miR-125 contains a synergistic effect with a similar miRNA cluster¹³. Moreover, miR-125 has the ability of lncRNA to repress the expression¹⁴.

In this study, we analyzed the effects of miR-125b on breast cancer cells by using the RNA-seq data. We figured out several DEGs and functional biological processes. We also introduced the gene enrichment and the protein-protein interaction (PPI) network to find the interacting molecules. The significant signaling found in our study will improve the treatment of breast cancer.

Methods

Data resources

Gene dataset GSE123358 was obtained from the GEO database. The data was produced by the Illumina HiSeq 2000 (Homo sapiens) (Special Histopathology Laboratory, National University of Singapore, Lvl 3, NUH Main Building, 5 Lower Kent Ridge Road, Kent Ridge, Singapore). The analyzed dataset includes 12 high miR-125b breast cancer cells (H) and 9 low miR-125b breast cancer cells (L).

Data acquisition and processing

The data were organized and conducted by R package as previously described^{15–17}. We used a classical t-test to identify DEGs with $P < 0.05$ and fold change ≥ 1.5 as being statistically significant.

The Kyoto Encyclopedia of Genes and Genomes (KEGG) and Gene Ontology (GO)

KEGG and GO analyses were conducted by R package (clusterProfiler) and Reactome. $P < 0.05$ was considered statistically significant.

Protein-protein interaction (PPI) networks

The Molecular Complex Detection (MCODE) was used to construct the PPI networks. The significant modules were produced from constructed PPI networks. The pathway analyses were performed by using Reactome (<https://reactome.org/>), and $P < 0.05$ was considered significant.

Results

Identification of DEGs by the impact of miR-125b on breast cancer cells

To determine the mechanism of miRNA-125b on the transcriptome of human breast cancer cells, we analyzed the sorted cells with maximum and minimum miR-125b expression. A total of 48 genes were identified with the threshold of $P < 0.05$. The top ten of up-and-down-regulated genes by the impact of miR-125b on cancer cells are identified by the heatmap and volcano plot (Figure 1). The top DEGs were indicated in Table 1.

Enrichment analysis of DEGs by the impact of miR-125b on breast cancer cells

To further analyze the mechanism of miR-125b impacted cancer cells, we analyzed the KEGG and GO enrichment (Figure 2). The top ten KEGG items include “Pathways of neurodegeneration – multiple diseases”, “Oxidative phosphorylation”, “Protein processing in endoplasmic reticulum”, “Parkinson disease”, “Alzheimer disease”, “Non-alcoholic fatty liver disease”, “Diabetic cardiomyopathy”, “Chemical carcinogenesis–reactive oxygen species”, “Thermogenesis”, “Nucleocytoplasmic transport”. We then identified the top ten biological processes “Maintenance of location”, “Striated muscle tissue development”, “Maintenance of location in cell”, “Protein-containing complex localization”, “Ubiquitin-dependent ERAD pathway”, “Mitochondrial electron transport, ubiquinol to cytochrome c”,

“Protein folding in endoplasmic reticulum”, “Lens morphogenesis in camera-type eye”, “Protein localization to endosome”, and “Regulation of protein sumoylation”. We also identified the top ten cellular components of GO including “Mitochondrial protein-containing complex”, “Inner mitochondrial membrane protein complex”, “Mitochondrial respirasome”, “Respiratory chain complex”, “Respirasome”, “Oxidoreductase complex”, “Mitochondrial respiratory chain complex III”, “Respiratory chain complex III”, “Endocytic vesicle lumen”, and “Endoplasmic reticulum quality control compartment”. We identified the top ten molecular functions of GO including “Transcription coregulator activity”, “Cadherin binding”, “Unfolded protein binding”, “Proton transmembrane transporter activity”, “Protein phosphatase binding”, “Transcription corepressor activity”, “Phosphatase binding”, “SMAD binding”, “Amyloid-beta binding”, and “Beta-catenin binding”.

PPI network construction

To further determine the relationship of the DEGs, we constructed the PPI network by String network and Cytoscape tool as described¹⁷⁻¹⁹. The combined score was set > 0.2 as a cutoff to construct the PPI network by using the 48 nodes and 32 edges. Table 2 showed the top ten molecules with the highest degree scores. The top two cluster modules were indicated in Figure 3. We further analyzed the DEGs and the PPI network by Reactome (Figure 4 and Supplemental Table S1). We also determined the top ten significant biological processes through Reactome map including “ATF6 (ATF6-alpha) activates chaperone genes”, “ATF6 (ATF6-alpha) activates chaperones”, “Respiratory electron transport, ATP synthesis by chemiosmotic coupling, and heat production by uncoupling proteins”, “Formation of ATP by chemiosmotic coupling”, “Response of EIF2AK1 (HRI) to heme deficiency”, “Cristae formation”, “The citric acid (TCA) cycle and respiratory electron transport”, “Unfolded Protein Response (UPR)”, and “Cellular responses to stress”.

Discussion

miRNAs play key roles in tumor development but are aberrantly expressed in cancers such as breast cancers. Feng Tang et al found miR-125b was positively correlated with the migratory ability of breast cancer cells by using gain and loss-of-function methods²⁰. However, the exact mechanisms of miR-125b treated breast cancer cells are still unknown.

The KEGG and GO analyses showed the mitochondria and endoplasmic reticulum oxidative phosphorylation pathways are important components in the miR-125b mediated breast cancer cells. Pamela Becherini et al found Sirtuin 6 (SIRT6) increases oxidative phosphorylation in breast cancer and enhances tumorigenesis in vivo study²¹. Isabelle Duroux-Richard et al found miR-125b regulates monocyte adaptation via mitochondrial metabolism and dynamics²². Interestingly, mitochondria metabolism involves various biological processes²³⁻²⁶, which is an effective target for cancer. Reprogramming metabolic pathways could ameliorate the metabolic inhibitors to suppress cancers, such as triple-negative breast cancer²⁷. The endoplasmic reticulum (ER) attributes to the maintenance of cellular functions including organelle and lipogenesis, which plays essential roles in the progression of

cancer^{28–30}. Milad Ashrafizadeh et al also found the autophagy and ER stress are promising methods to treat breast cancer³¹.

Base on the findings of KEGG and GO, we also identified ten significant molecules that involve in the miR-125b mediated breast cancer. UQCRQ was identified as the significant protein in triple-negative breast cancer³². Eduardo Cruz-Ramos et al found the CALR levels were increased in breast cancer cells lacking estrogen receptor alpha (ER α), in comparison with those that express ER α ³³. G-protein-coupled receptors (GPCRs) and Regulators of G protein signaling (RGS) are key regulators that modulate a variety of human diseases including arthritis, bone, and heart diseases^{34–43}. Interestingly, calreticulin has been found to interact with several GPCR proteins such as AT1R and V2R⁴⁴. Jiawei Zhou et al found HNRNPU enhances epithelial-mesenchymal transition, invasion capacity but represses the viability of invasive breast carcinoma cells⁴⁵. Circadian gene clocks and their target genes are involved in a number of cell functions including proliferation, differentiation, metabolism, migration, and secretion^{46–50}. Beibei Lai et al found HNRNPU is expressed in a circadian manner in the suprachiasmatic nucleus, which can be regulated by the circadian genes⁵¹. Penn Muluhngwi et al found ATP5G1 was identified as a target of miRNA in breast cancer⁵². A study by Radhakrishnan Vishnubalaji found that the lack of function of NDUFB11 repressed the triple-negative breast cancer and enhanced its sensitivity to paclitaxel⁵³. Kjerstin M Owens et al found UQCRH was increased in human breast cancers⁵⁴. Thomas R Cawthorn et al found HSP90B1 is related to breast cancer metastasis by performing the proteomic analyses⁵⁵. TGOLN2 and SAP18 were found to be closely related to the miRNA treatment in normal or tumor tissues^{56, 57}. Jianwei Lin et al found the increased XPOT showed a poor prognosis in patients with breast cancer⁵⁸.

In conclusion, this study showed the impact of miR-125b on breast cancer. The mitochondria and endoplasmic reticulum oxidative phosphorylation pathways are mainly processes in miR-125b mediated breast cancer. Therefore, this study may be beneficial in the treatment of breast cancer by using miR-125b.

Declarations

Author Contributions

Hongmei Guo, Wei Zhang, Guangqi Liu, Tingxiang Chang: Methodology. Hanming Gu: Conceptualization, Writing and Editing.

Funding

This work was not supported by any funding.

Declarations of interest

There is no conflict of interest to declare.

References

1. Rivenbark AG, O'Connor SM, Coleman WB: Molecular and cellular heterogeneity in breast cancer: challenges for personalized medicine. *Am J Pathol* 2013, 183:1113–24.
2. Schirmacher V: From chemotherapy to biological therapy: A review of novel concepts to reduce the side effects of systemic cancer treatment (Review). *Int J Oncol* 2019, 54:407–19.
3. Sciaraffa T, Guido B, Khan SA, Kulkarni S: Breast cancer risk assessment and management programs: A practical guide. *Breast J* 2020, 26:1556–64.
4. Djulbegovic B, Kumar A, Soares HP, Hozo I, Bepler G, Clarke M, Bennett CL: Treatment success in cancer: new cancer treatment successes identified in phase 3 randomized controlled trials conducted by the National Cancer Institute-sponsored cooperative oncology groups, 1955 to 2006. *Arch Intern Med* 2008, 168:632–42.
5. Valastyan S, Weinberg RA: Tumor metastasis: molecular insights and evolving paradigms. *Cell* 2011, 147:275–92.
6. Shrestha A, Martin C, Burton M, Walters S, Collins K, Wyld L: Quality of life versus length of life considerations in cancer patients: A systematic literature review. *Psychooncology* 2019, 28:1367–80.
7. Moazed D: Small RNAs in transcriptional gene silencing and genome defence. *Nature* 2009, 457:413–20.
8. Han J, Lee Y, Yeom KH, Kim YK, Jin H, Kim VN: The Drosha-DGCR8 complex in primary microRNA processing. *Genes Dev* 2004, 18:3016–27.
9. Macfarlane LA, Murphy PR: MicroRNA: Biogenesis, Function and Role in Cancer. *Curr Genomics* 2010, 11:537–61.
10. Slezak-Prochazka I, Durmus S, Kroesen BJ, van den Berg A: MicroRNAs, macrocontrol: regulation of miRNA processing. *RNA* 2010, 16:1087-95.
11. Bartel DP: MicroRNAs: target recognition and regulatory functions. *Cell* 2009, 136:215–33.
12. Oliveto S, Mancino M, Manfrini N, Biffo S: Role of microRNAs in translation regulation and cancer. *World J Biol Chem* 2017, 8:45–56.
13. Wang Y, Zeng G, Jiang Y: The Emerging Roles of miR-125b in Cancers. *Cancer Manag Res* 2020, 12:1079–88.
14. Statello L, Guo CJ, Chen LL, Huarte M: Gene regulation by long non-coding RNAs and its biological functions. *Nat Rev Mol Cell Biol* 2021, 22:96–118.
15. Yu G, Wang LG, Han Y, He QY: clusterProfiler: an R package for comparing biological themes among gene clusters. *OMICS* 2012, 16:284–7.

16. Li J, Wang W, Gu H: Identification of biological processes and signaling pathways for the knockout of REV-ERB in mouse brain. *bioRxiv* 2021:2021.11.22.469579.
17. Zhang M, Wang J, Gu H: Identification of biological processes and signaling pathways in the stretched nucleus pulposus cells. *bioRxiv* 2021:2021.11.23.469730.
18. Hanming G, Wei W, Gongsheng Y: Identification of potential biomarkers and inhibitors in SARS-CoV-2 infected macaques. *Research Square* 2020.
19. Gu H, Wang W, Yuan G: Identification of biomarkers and candidate inhibitors for multiple myeloma. *bioRxiv* 2021:2021.02.25.432847.
20. Tang F, Zhang R, He Y, Zou M, Guo L, Xi T: MicroRNA-125b induces metastasis by targeting STARD13 in MCF-7 and MDA-MB-231 breast cancer cells. *PLoS ONE* 2012, 7:e35435.
21. Becherini P, Caffa I, Piacente F, Damonte P, Vellone VG, Passalacqua M, Benzi A, Bonfiglio T, Reverberi D, Khalifa A, Ghanem M, Guijarro A, Tagliafico L, Sucameli M, Persia A, Monacelli F, Cea M, Bruzzzone S, Ravera S, Nencioni A: SIRT6 enhances oxidative phosphorylation in breast cancer and promotes mammary tumorigenesis in mice. *Cancer Metab* 2021, 9:6.
22. Duroux-Richard I, Roubert C, Ammari M, Presumey J, Grun JR, Haupl T, Grutzkau A, Lecellier CH, Boitez V, Codogno P, Escoubet J, Pers YM, Jorgensen C, Apparailly F: miR-125b controls monocyte adaptation to inflammation through mitochondrial metabolism and dynamics. *Blood* 2016, 128:3125–36.
23. Yuan G: Identification of biomarkers and pathways of mitochondria in sepsis patients. *bioRxiv* 2021:2021.03.29.437586.
24. Xu L, Cheng Q, Hua B, Cai T, Lin J, Yuan G, Yan Z, Li X, Sun N, Lu C, Qian R: Circadian gene Clock regulates mitochondrial morphology and functions by posttranscriptional way. *bioRxiv* 2018:365452.
25. Yuan G, Yang S, Liu M, Yang S: RGS12 is required for the maintenance of mitochondrial function during skeletal development. *Cell Discov* 2020, 6:59.
26. Cai T, Hua B, Luo D, Xu L, Cheng Q, Yuan G, Yan Z, Sun N, Hua L, Lu C: The circadian protein CLOCK regulates cell metabolism via the mitochondrial carrier SLC25A10. *Biochim Biophys Acta Mol Cell Res* 2019, 1866:1310–21.
27. Lee J, Yesilkanal AE, Wynne JP, Frankenberger C, Liu J, Yan J, Elbaz M, Rabe DC, Rustandy FD, Tiwari P, Grossman EA, Hart PC, Kang C, Sanderson SM, Andrade J, Nomura DK, Bonini MG, Locasale JW, Rosner MR: Effective breast cancer combination therapy targeting BACH1 and mitochondrial metabolism. *Nature* 2019, 568:254–8.
28. Wang Y, Wang K, Jin Y, Sheng X: Endoplasmic reticulum proteostasis control and gastric cancer. *Cancer Lett* 2019, 449:263–71.
29. Yuan G, Hua B, Cai T, Xu L, Li E, Huang Y, Sun N, Yan Z, Lu C, Qian R: Clock mediates liver senescence by controlling ER stress. *Aging* 2017, 9:2647–65.
30. Fan XF, Wang XR, Yuan GS, Wu DH, Hu LG, Xue F, Gong YS: [Effect of safflower injection on endoplasmic reticulum stress-induced apoptosts in rats with hypoxic pulmonary hypertension]. *Zhongguo Ying Yong Sheng Li Xue Za Zhi* 2012, 28:561–7.

31. Ashrafizadeh M, Mohammadinejad R, Tavakol S, Ahmadi Z, Sahebkar A: New Insight into Triple-Negative Breast Cancer Therapy: The Potential Roles of Endoplasmic Reticulum Stress and Autophagy Mechanisms. *Anticancer Agents Med Chem* 2021, 21:679–91.
32. He J, Yang J, Chen W, Wu H, Yuan Z, Wang K, Li G, Sun J, Yu L: Molecular Features of Triple Negative Breast Cancer: Microarray Evidence and Further Integrated Analysis. *PLoS ONE* 2015, 10:e0129842.
33. Cruz-Ramos E, Sandoval-Hernandez A, Tecalco-Cruz AC: Differential expression and molecular interactions of chromosome region maintenance 1 and calreticulin exportins in breast cancer cells. *J Steroid Biochem Mol Biol* 2019, 185:7–16.
34. Yuan G, Huang Y, Yang S-t, Ng A, Yang S: RGS12 inhibits the progression and metastasis of multiple myeloma by driving M1 macrophage polarization and activation in the bone marrow microenvironment. *Cancer Commun*, n/a.
35. Yuan G, Fu C, Yang ST, Yuh DY, Hajishengallis G, Yang S: RGS12 Drives Macrophage Activation and Osteoclastogenesis in Periodontitis. *J Dent Res* 2021:220345211045303.
36. Fu C, Yuan G, Yang ST, Zhang D, Yang S: RGS12 Represses Oral Cancer via the Phosphorylation and SUMOylation of PTEN. *J Dent Res* 2020:22034520972095.
37. Mao SZ, Fan XF, Xue F, Chen R, Chen XY, Yuan GS, Hu LG, Liu SF, Gong YS: Intermedin modulates hypoxic pulmonary vascular remodeling by inhibiting pulmonary artery smooth muscle cell proliferation. *Pulm Pharmacol Ther* 2014, 27:1–9.
38. Yuan G, Yang S, Gautam M, Luo W, Yang S: Macrophage regulator of G-protein signaling 12 contributes to inflammatory pain hypersensitivity. *Ann Transl Med* 2021, 9:448.
39. Yuan G, Yang S, Yang S: Macrophage RGS12 contributes to osteoarthritis pathogenesis through enhancing the ubiquitination. *Genes & Diseases* 2021.
40. Hanming G: nuotrophils arthritis. *Research Square* 2021.
41. Yuan G, Yang S, Yang S, Ng A, Oursler MJ: RGS12 is a critical proinflammatory factor in the pathogenesis of inflammatory arthritis via acting in Cox2-RGS12-NF kappa B pathway activation loop. *J Bone Miner Res: WILEY 111 RIVER ST, HOBOKEN 07030-5774, NJ USA*, 2019. pp. 147-.
42. Sun L, Ye RD: Role of G protein-coupled receptors in inflammation. *Acta Pharmacol Sin* 2012, 33:342–50.
43. Yuan G, Yang S, Ng A, Fu C, Oursler MJ, Xing L, Yang S: RGS12 Is a Novel Critical NF-kappaB Activator in Inflammatory Arthritis. *iScience* 2020, 23:101172.
44. Dong C, Filipeanu CM, Duvernay MT, Wu G: Regulation of G protein-coupled receptor export trafficking. *Biochim Biophys Acta* 2007, 1768:853–70.
45. Zhou J, Guo Y, Huo Z, Xing Y, Fang J, Ma G, Han Q, Wang M, Xu Q: Identification of therapeutic targets and prognostic biomarkers from the hnRNP family in invasive breast carcinoma. *Aging* 2021, 13:4503–21.
46. Zhu Z, Hua B, Xu L, Yuan G, Li E, Li X, Sun N, Yan Z, Lu C, Qian R: CLOCK promotes 3T3-L1 cell proliferation via Wnt signaling. *IUBMB Life* 2016, 68:557–68.

47. Yuan G, Hua B, Yang Y, Xu L, Cai T, Sun N, Yan Z, Lu C, Qian R: The Circadian Gene Clock Regulates Bone Formation Via PDIA3. *J Bone Miner Res* 2017, 32:861–71.
48. Zhu Z, Hua B, Shang Z, Yuan G, Xu L, Li E, Li X, Sun N, Yan Z, Qian R, Lu C: Altered Clock and Lipid Metabolism-Related Genes in Atherosclerotic Mice Kept with Abnormal Lighting Condition. *Biomed Res Int* 2016, 2016:5438589.
49. Yuan G, Xu L, Cai T, Hua B, Sun N, Yan Z, Lu C, Qian R: Clock mutant promotes osteoarthritis by inhibiting the acetylation of NFkappaB. *Osteoarthritis Cartilage* 2019, 27:922–31.
50. Zhu Z, Xu L, Cai T, Yuan G, Sun N, Lu C, Qian R: Clock represses preadipocytes adipogenesis via GILZ. *J Cell Physiol* 2018, 233:6028–40.
51. Lai B, Zou J, Lin Z, Qu Z, Song A, Xu Y, Gao X: Haploinsufficiency of hnRNP U Changes Activity Pattern and Metabolic Rhythms. *Am J Pathol* 2018, 188:173–83.
52. Muluhngwi P, Alizadeh-Rad N, Vittitow SL, Kalbfleisch TS, Klinge CM: The miR-29 transcriptome in endocrine-sensitive and resistant breast cancer cells. *Sci Rep* 2017, 7:5205.
53. Vishnubalaji R, Alajez NM: Transcriptional landscape associated with TNBC resistance to neoadjuvant chemotherapy revealed by single-cell RNA-seq. *Mol Ther Oncolytics* 2021, 23:151–62.
54. Owens KM, Kulawiec M, Desouki MM, Vanniarajan A, Singh KK: Impaired OXPHOS complex III in breast cancer. *PLoS ONE* 2011, 6:e23846.
55. Cawthorn TR, Moreno JC, Dharsee M, Tran-Thanh D, Ackloo S, Zhu PH, Sardana G, Chen J, Kupchak P, Jacks LM, Miller NA, Youngson BJ, Iakovlev V, Guidos CJ, Vallis KA, Evans KR, McCready D, Leong WL, Done SJ: Proteomic analyses reveal high expression of decorin and endoplasmin (HSP90B1) are associated with breast cancer metastasis and decreased survival. *PLoS ONE* 2012, 7:e30992.
56. Yang H, Su H, Hu N, Wang C, Wang L, Giffen C, Goldstein AM, Lee MP, Taylor PR: Integrated analysis of genome-wide miRNAs and targeted gene expression in esophageal squamous cell carcinoma (ESCC) and relation to prognosis. *BMC Cancer* 2020, 20:388.
57. Farhana L, Dawson MI, Fontana JA: Down regulation of miR-202 modulates Mxd1 and Sin3A repressor complexes to induce apoptosis of pancreatic cancer cells. *Cancer Biol Ther* 2015, 16:115–24.
58. Lin J, Hou Y, Huang S, Wang Z, Sun C, Wang Z, He X, Tam NL, Wu C, Wu L: Exportin-T promotes tumor proliferation and invasion in hepatocellular carcinoma. *Mol Carcinog* 2019, 58:293–304.

Tables

Tables 1-2 are in the supplementary files section.

Figures

Figure 1

Heatmap and volcano plot were obtained from the low and high expression of miR-125b in breast cancer cells

- (A) Heatmap of significant differentially expressed genes (DEGs). Significant DEGs ($P < 0.01$) were used to create the heatmap.
- (B) Volcano plot for DEGs from the low and high expression of miR-125b in breast cancer cells. The mostly changed genes are highlighted by grey dots.

Figure 2

KEGG and GO analyses of DEGs from the low and high expression of miR-125b in breast cancer cells

- (A) KEGG analysis, (B) Biological processes, (C) Cellular components, (D) Molecular functions.

Figure 3

The PPI network analysis of DEGs from the low and high expression of miR-125b in breast cancer cells

- Cluster 1 (A) and cluster 2 (B) were the top two clusters and were constructed by MCODE in Cytoscape.

Figure 4

Reactome map representation of the significant biological processes from the low and high expression of miR-125b in breast cancer cells

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementalTableS1.xlsx](#)
- [Tables.docx](#)