MEDS Clinical Medicine (2021) 2: 27-32
Clausius Scientific Press, Canada

DOI: 10.23977/medsc.2021.020105
ISSN ISSN 2616-1907

Hsa-Mir-29b-3p Inhibits Biological Development of Cancer by Targeting Inhibiting Expression of Cav2

BAI Wen-juan[1], LIU Yu[2,*]

[1]Department of Biochemistry, College of Lab Medicine, Hebei North University, Zhangjiakou 075000, China

[2]Laboratory Animal Center, Hebei North University, Zhangjiakou 075000, China

**Corresponding Author*

Keywords: Bioinformatics, Lung adenocarcinoma, Hyaluronic acid, Prognostic genes

Abstract: Objective: To determine the role of hsa-miR-29b-3p in lung adenocarcinoma. Methods: Download miRNA mature for TCGA-LUAD, mRNA. from TCGA Database Differ differential analysis of miR-29b-3p based on the downloaded data obtained the differential gene expression matrix of miRNA and mRNA, and then intersects with the target genes predicted by multiple databases to obtain the target gene. Further KEGG enrichment analysis was performed on the target gene.Result:miR-29b-3p is significantly highly expressed in tumor tissue, its downstream regulated lower expression of the target gene CAV2 in cancer, and its lower expression indicates a better prognosis. KEGG enrichment results indicate significant enrichment of CAV2 in syndecan 2 pathway, Proteoglycans in cancer, ESR-mediated signaling, Signaling by Nuclear Receptors, Signal Transduction etc in Pathways associated with signal transduction and cell processes. Conclusion:hsa-miR-29b-3p suppresses cancer cell proliferation, adhesion, angiogenesis an d metastasis, helping to inhibit the development of lung adenocarcinoma and can be used a s a new therapeutic target.

1. Introduction

Lung adenocarcinoma is a type of non-small cell cancer that is more likely to occur in women and non-smokers. It originates from the bronchial mucosal epithelium, most from the smaller bronchial, and a few from the larger mucus glands. The age of onset is younger, and women are relatively common. Early generally no obvious clinical symptoms, difficult to find early, prone to metastasis.

It has been shown in the relevant literature that circHYBID up-regulates the expression of conver ting growth factor- β1 through sponge hsa-miR-29b-3p, while circHYBID overexpression in chondr ocytes increases the accumulation of hyaluronic acid by regulating hyaluronic acid synthase 2 and HYBID expression[1]. As is generally known, hyaluronic acid is the main component of the extrace llular matrix of value-added cells and migratory cells. The hydration space formed by hyaluronic ac id helps keep cells separate from each other, making cells easy to move and increase value.

In this study, in order to find out the core genes associated with lung adenocarcinoma. The lung

adenocarcinoma dataset and clinical data from the TCGA database were used to screen out key core genes. Analysis provides the potential prognosis of genes for lung adenocarcinoma and will help to study the occurrence and development of lung adenocarcinoma.

2. Materials and Methods

2.1 Data Download and Pretreatment

Expression data for TCGA-LUAD's miRNA maturation (46 normal samples, 521 cancer samples) and 59 normal mRNA(normal samples and 535 cancer samples) were downloaded from the TCGA database. Expression analysis of miR-29b-3p based on download data. EdgeR for mRNA (|logFC|> 2.0, padj <0.01) for DEGs(Differentially Expressed Genes).

2.2 Targeted Prediction

Target hsa-miR-29b-3p was targeted using targetScan, miRDB, miDIP and starBase databases, crossing the target genes predicted by multiple databases with the downregulation genes of mRNA.

2.3 Correlation Analysis

The obtained gene and hsa-miR-29b-3p used Pearson correlation analysis using R language, and mRNA with the highest negative correlation was selected as the subjects.

2.4 Ppi Network Analysis

PPI network analysis of target mRNA using string website and cytoscape software.

2.5 Prognostic Analysis

Expression analysis using ggpubr packages in the R language, survival analysis using survival and qvalue packages, and expression analysis at different stages.

2.6 Enrichment Analysis.

KEGG, GSEA enrichment analysis of target genes using R Language and GSEA.

3. Results and Discussion

Extensive work suggests that hsa-miR-29b-3p plays an important role in regulating the pathogenesis of cancer. It is downregulated in gastric cancer[2], in colorectal cancer[3], and can regulate multiple pathways and affect cellular processes, inhibit the biological development of multiple cancers, and can serve as prognostic markers. So miR-139-5p was selected as the subject to clarify its role in lung adenocarcinoma and other cancers. For difference analysis using EdgeR, 2502 DEGs, were raised by 1974 and 528 (Figure 1 a,b).

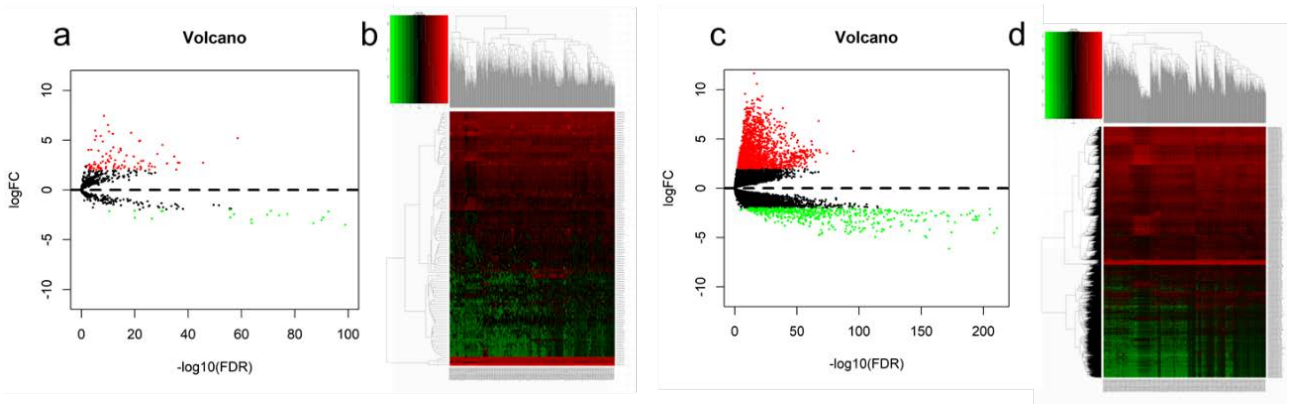

Fig.1 A,B Thermal Map of Mirna in Tcga-Luad. C,d Thermal Map of Mrna of Tcga-Luad

TCGA-LUAD data suggest a significant upregulation of hsa-miR-29b-3p in lung adenocarcinoma (Figure 2a).To increase predictive credibility, target gene prediction for hsa-miR-29b-3p was performed using 4 databases of targetScan, miRDB, miDIP and starBase. Based on the ceRNA hypothesis, miRNA should be negatively associated with the target gene mRNA. Therefore, the down-regulated genes of the predicted target gene expression matrix were crossed and obtained NCKAP 5, HBE GF, CAV 2 and KLF4 (Figure 2b). Pearson was analyzed with the predicted target gene and the highest negative correlation CAV2 was selected as the target (Figure 2c,d).

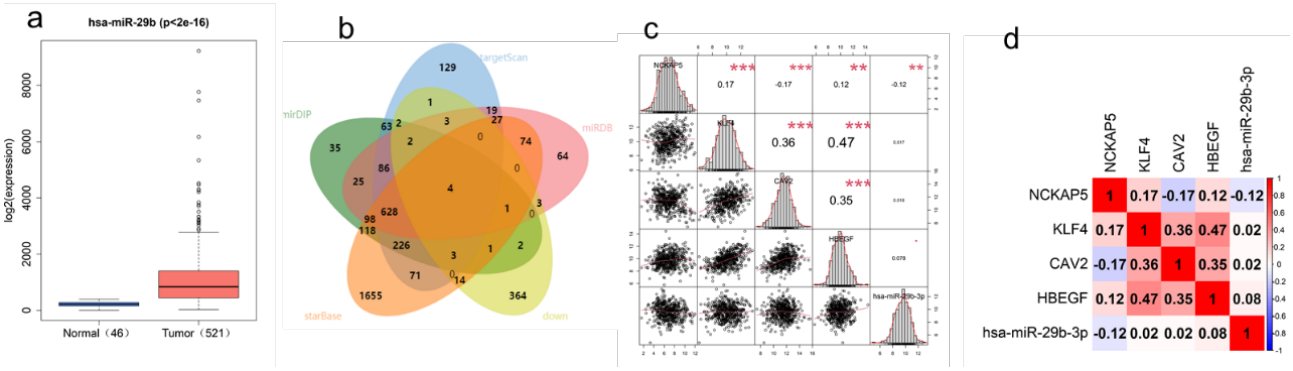

Figure 2 a miR-139-5p expression quantity box line diagram. b Prediction miR-139-5p target genes and differences upregulate mRNA intersection using miRDB, miDIP and starBase databases. c,d miR-139-5p and predicgene Pearson.

Using string and cytoscape (Figure 3a,b), the protein interaction network analysis shows that where CAV2 is the core gene.

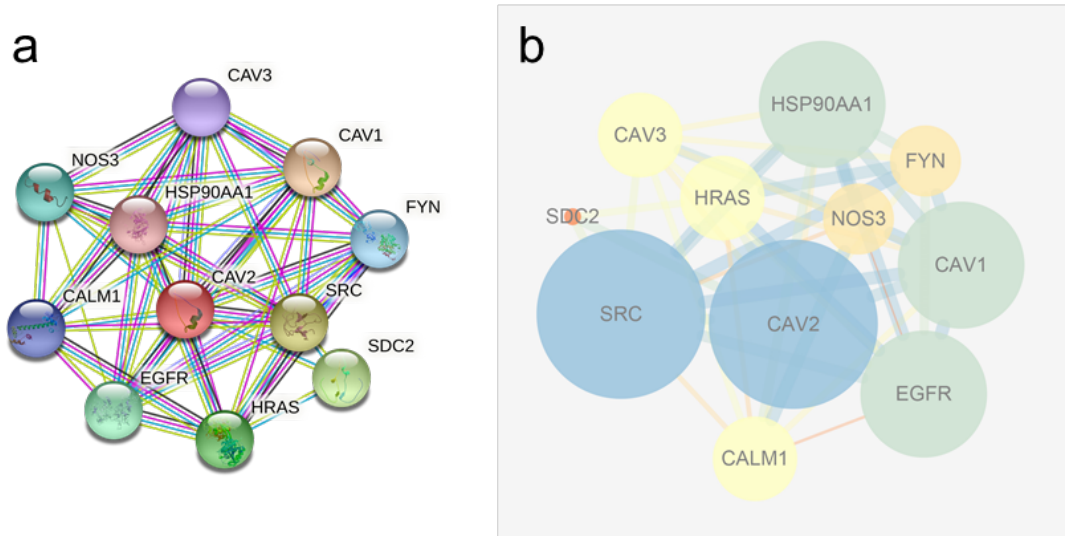

Fig.3 A,B Protein Interoperability Network Analysis.

The analysis showed that CAV2 was significantly low in lung adenocarcinoma tissue (Figure 4a) and generally higher overall survival of patients with low-expressed lung adenocarcinoma (Figure 4b). Furthermore, the expression of CAV2 at different stages (Figure 4c).However, mutations in CAV2 show the rise in different stages of lung adenocarcinoma, and the high expression of CAV2 indicates a poor prognosis.

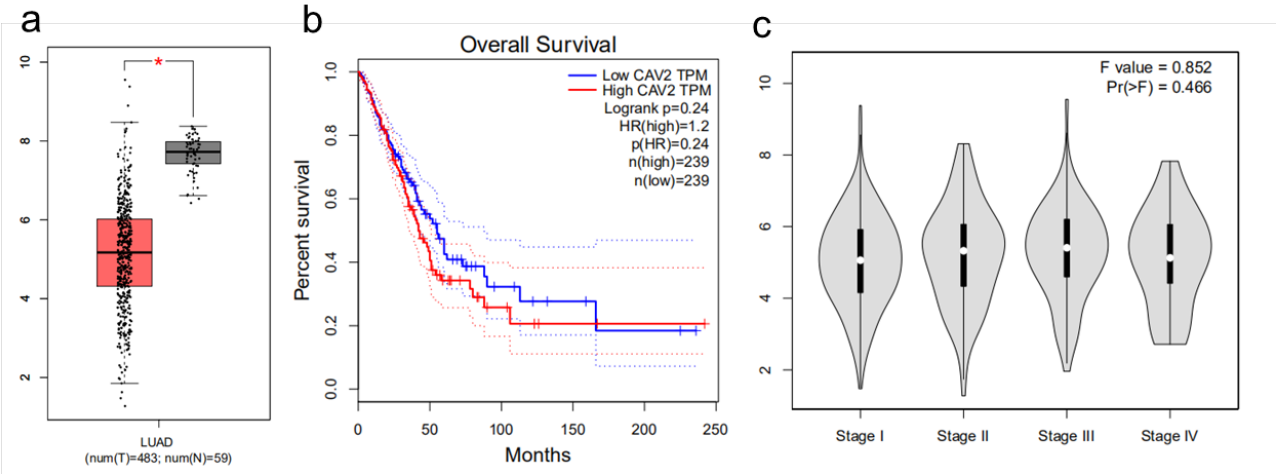

Figure 4 a Expression quantity box line diagram of CAV2. b The survival curve of the CAV2 gene, horizontal coordinates mean time (in years), vertical coordinates for survival, red curve means high expression, and blue curve means low expression. c CAV2 expression at different stages of lung cancer.

A KEGG enrichment analysis of the CAV2, The results showed that CAV2 was significantly enriched to Focal adhesion, syndecan 2 pathway, Proteoglycans in cancer, ESR-mediated signaling, Signaling by Nuclear Receptors, Signal Transduction, Extra-nuclear estrogen signaling and channels associated with cell cycle, cell processes, metabolic pathways, and signaling transduction (Figure 5).

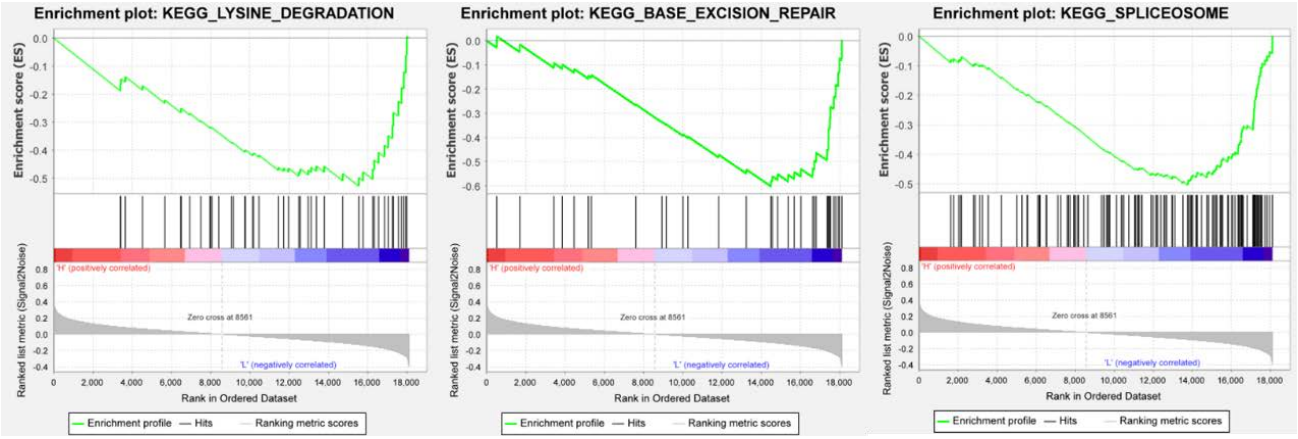

Fig.5 Low Expression Group of Gsea Enrichment Analysis.

It is understood in gene cards that the CAV2 gene encoded protein are the main components of th e subconcave inner surface of the cell membrane and participate in basic cell functions such as sign al transduction, cell growth control, and apoptosis.This protein may function as a tumor suppressor. This gene and related family member (CAV1) are located next to each other on chromosome 7, and express colocalizing proteins that form a stable hetero-oligomeric complex. Alternatively spliced transcript variants encoding different isoforms have been identified for this gene.[4]

High expression of CAV2 is associated with cancer progression. overexpression of CAV2 in panc reatic cancer promotes progression and metastasis of pancreatic cancer and showed a poor prognosi s[5].In renal cell cancer, CAV2 promotes the cancer growth of renal cell cancer through the EGFR / PI3K / Akt pathway, while CAV2 silence inhibits the proliferation, migration, and invasion of renal cell cancer cells[6]. In glioma, miRNA-144 inhibits the development of glioma by targeting CAV2[7].Some other literature has shown that CAV2 is associated with primary tumors and lymph node m etastasis[8]. Through the above proof that CAV2 is closely related to the development of cancer, it i s here speculated that it can promote cancer development when CAV2 is overexpressed, and when t he expression of silent CAV2 can inhibit cancer development.

By finding the relevant literature, hsa-miR-29b-3p has been shown to be associated with the accu mulation of hyaluronic acid, which is greatly related to cell migration. In this paper, miR-29b-3p in hibited the expression of CAV2 by targeting CAV2, thus inhibiting the development of lung adenoc arcinoma. Therefore, the CAV2 can act as a potential target factor.

4. Conclusion

In conclusion, it is speculated that the up-gulation of hsa-miR-29b-3p can target inhibiting CAV2 expression and thus inhibit cancer cell proliferation, adhesion, angiogenesis and metastasis, which is helpful to inhibit the development of lung adenocarcinoma and can be used as a new therapeutic target.

References

[1] Liao HX, Zhang ZH, Chen HL, Huang YM, Liu ZL, Huang J. CircHYBID regulates hyaluronan metabolism in chondrocytes via hsa-miR-29b-3p/TGF-β1 axis. Mol Med. 2021 May 31;27(1):56.

[2] Bai ZM, Li XF, Yang Y, Yang YF, Lv DR, Tang LL. Propofol inhibited gastric cancer proliferation via the hsa-miR-328-3p/STAT3 pathway. Clin Transl Oncol. 2021 Mar 27.

[3] Li C, Wang P, Du J, Chen J, Liu W, Ye K. LncRNA RAD51-AS1/miR-29b/c-3p/NDRG2 crosstalk repressed proliferation, invasion and glycolysis of colorectal cancer. IUBMB Life. 2021 Jan;73(1):286-298.

[4] Fujimoto T, Kogo H, Ishiguro K, Tauchi K, Nomura R. Caveolin-2 is targeted to lipid droplets, a new "membrane

domain" in the cell. J Cell Biol. 2001 Mar 5;152(5):1079-85.

[5] Zhu Y, Tian J, Peng X, Wang X, Yang N, Ying P, Wang H, Li B, Li Y, Zhang M, Cai Y, Lu Z, Niu S, Li Y, Zhong R, Chang J, Miao X. A genetic variant conferred high expression of CAV2 promotes pancreatic cancer progression and associates with poor prognosis. Eur J Cancer. 2021 Jul;151:94-105.

[6] Liu F, Shangli Z, Hu Z. CAV2 promotes the growth of renal cell carcinoma through the EGFR/PI3K/Akt pathway. Onco Targets Ther. 2018 Sep 25;11:6209-6216.

[7] Liu ZQ, Ren JJ, Zhao JL, Zang J, Long QF, Du JJ, Jia XT, Gu NB, Di ZL, Qian YH, Li SZ. MicroRNA-144 represses gliomas progression and elevates susceptibility to Temozolomide by targeting CAV2 and FGF7. Sci Rep. 2020 Mar 5;10(1):4155.

[8] Gerstenberger W, Wrage M, Kettunen E, Pantel K, Anttila S, Steurer S, Wikman H. Stromal Caveolin-1 and Caveolin-2 Expression in Primary Tumors and Lymph Node Metastases. Anal Cell Pathol (Amst). 2018 Apr 10;2018:8651790.