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LncRNA PCBP1-AS1 suppresses cell growth in oral squamous cell carcinoma by targeting miR-34c-5p/ZFP36 axis

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Abstract

Oral squamous cell carcinoma (OSCC) is the most frequently diagnosed oral malignancy and poses a great threat to public health. According to bioinformatics analysis, long noncoding RNA PCBP1-AS1 is downregulated in OSCC. In this work, the functions and mechanism of PCBP1-AS1 in OSCC were further investigated. PCBP1-AS1 expression in OSCC cells was measured by quantitative polymerase chain reaction. Cell viability and proliferation were detected using CCK-8 assays and colony-forming assays. TUNEL assays as well as flow cytometry analyses were carried out to detect OSCC cell apoptosis. Binding relationship between PCBP1-AS1 and miR-34c-5p or that between miR-34c-5p and ZFP36 in OSCC cells was identified using RNA immunoprecipitation assays, RNA pulldown assays, and luciferase reporter assays. Experimental results revealed that PCBP1-AS1 was downregulated in OSCC cells. PCBP1-AS1 overexpression hampered cell proliferation and enhanced cell apoptosis in OSCC. PCBP1-AS1 interacted with miR-34c-5p in OSCC and negatively regulated miR-34c-5p. ZFP36 3'untranslated region was targeted by miR-34c-5p. PCBP1-AS1 positively regulated ZFP36 expression. ZFP36 silencing abrogated the suppressive impact of PCBP1-AS1 on OSCC cell growth. In summary, PCBP1-AS1 suppresses cell growth in OSCC by upregulating ZFP36 through interaction with miR-34c-5p.

Keywords: PCBP1-AS1, Oral squamous cell carcinoma, miR-34c-5p, ZFP36, ceRNA

1. Introduction

OSCC is a heterogeneous cancer that occurs in the mucosal lining of the oral cavity [1-3]. Lifestyle habits such as alcohol intake and smoking are responsible for OSCC tumorigenesis [4]. OSCC correlates with a high mortality rate and is prevalent worldwide, with over 300, 000 patients diagnosed annually [5, 6]. Current treatments for patients with OSCC include biologic therapy, chemotherapy, surgery, and radiotherapy [6]. However, the treatment outcomes of OSCC patients are largely unfavorable [7]. There is a clear need to make an early and accurate diagnosis. Understanding the molecular mechanism underlying OSCC is of great significance in improving the prognosis of patients.

Long noncoding RNAs (lncRNAs) are crucial factors for the initiation and development of OSCC [8-10]. LncRNAs are consisted of over 200 nucleotides and have limited protein-coding capability [11], which participate in the initiation and metastasis of tumors by regulating various biological behaviors [12]. For instance, knockdown of lncRNA CASC9 facilitates cell autophagy while inhibiting cell proliferation [13]. Moreover, silencing of lncRC3H2 inhibits OSCC cell growth and metastasis *in vitro* [14]. LINC00657, remarkably upregulated in OSCC tissues, shows a close association with the poor prognosis of OSCC patients [15].

Based on bioinformatics databases, PCBP1-AS1 level is lessened in head and neck squamous cell carcinoma (HNSC) samples, which is correlated to poor prognosis of patients. In addition, the aberrant expression of PCBP1-AS1 in OSCC has also been mentioned in previous studies [16]. However, the underpinning mechanism of PCBP1-AS1 in OSCC has not been reported yet. Previously, PCBP1-AS1 level was reported to be reduced in lung adenocarcinoma, and its knockdown facilitates cancer cell invasion and migration [17]. PCBP1-AS1 is high-expressed in hepatocellular carcinoma and promotes proliferation and metastasis via regulation of PCBP1 and downstream signaling [18]. Moreover, PCBP1-AS1 was reported to be involved in the competing endogenous RNA (ceRNA) network in Hodgkin lymphoma [19].

According to the ceRNA hypothesis, lncRNAs can interact with microRNAs (miRNAs) in a competitive manner to regulate expression levels of protein-coding genes

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[20]. The ceRNA role of lncRNAs in OSCC has been widely investigated. For example, JPX/miR-944/CDH2 network, LHFPL3-AS1/miR-362-5p/CHSY1 network, and LINC01929/miR-137-3p/FOXC1 network are newly reported ceRNA hypothesis in OSCC [21-23]. We suspected that PCBP1-AS1 may serve as a ceRNA in OSCC to regulate downstream genes.

The functions and mechanisms of PCBP1-AS1 in OSCC were explored in the study. The study may lay a therapeutical basis for OSCC diagnosis and prognosis.

2. Materials and methods

2.1. Cell lines

OSCC cell lines (CAL-27, SCC-15, and SCC-9) and oral normal epithelial cell line (NHOK) purchased from Chinese Academy of Sciences (Shanghai, China) were maintained in culture medium (RPMI 1640, Sigma-Aldrich, USA) containing fetal bovine serum (10%), streptomycin (100 μg/mL), and penicillin (100 U/mL) at 37°C with 5% CO_2.

2.2. Transfections

miR-34c-5p inhibitor/mimics, small interfering (si) RNA against PCBP1-AS1 (si-PCBP1-AS1#1/2) or ZFP36 (si-ZFP36), pCDH vector containing PCBP1-AS1 sequence and related negative control (NC) inhibitor/mimics, si-NC, and empty pCDH vector were obtained from GenePharma (Shanghai, China). Lipofectamine 3000 reagent (Invitrogen, USA) was used for 48 h cell transfection.

2.3. RT-qPCR

TRIzol Reagent (Invitrogen, USA) and PrimeScript™ RT reagent (Takara Bio, China) were adopted for RNA extraction and cDNA synthesis. qPCR was performed using SYBR Green PCR Master Mix (MedChem Express, USA) on the ABI 7900 thermocycler (Thermo Fisher, USA). GAPDH and U6 acted as endogenous controls for lncRNA/mRNAs and miRNAs, respectively. The $2^{-\Delta\Delta Ct}$ method was adopted to calculate relative gene expression.

2.4. Subcellular fractionation assay

PARIS kit (Life Technologies, USA) as well as Ambion's RNA isolation system (Life Technologies, USA) were utilized for isolation and purification of cytoplasmic and nuclear RNA from OSCC cells. PCBP1-AS1 levels in cytoplasmic and nuclear parts were determined utilizing qPCR analysis and normalized to U6 and GAPDH, respectively.

2.5. CCK-8 assay

After plated on 96-well plates (5000 cells/well), OSCC cells were cultured for 24, 48, 72 and 96 h. At these time points, Cell Counting Kit-8 kit was added into each well. Values of optical density (OD) were recorded adopting a microplate reader (BioTek, USA) at 450 nm wavelength.

2.6. Colony forming assay

Transfected CAL-27 and SCC-9 cells were plated to 6-well plates (500 cells/well) for 14 days of incubation. The medium was changed each three days. Next, formed colonies were treated with paraformaldehyde (4%, 30 min) and crystal violet solution (0.5%, 5 min), respectively, for fixing and staining. At last, number of cell colonies was calculated manually.

2.7. TUNEL assay

After washed with phosphate buffered saline twice, transfected CAL-27 and SCC-9 cells were fixed with 4% paraformaldehyde and permeabilized utilizing Triton-X 100 (0.25%, 25 min). Next, TUNEL assay reagent (Merck KGaA, Germany) was added to cells for incubation conforming to the manufacturer's protocols. After added with DAPI solution, nuclei were stained in blue. An optical microscopy (Olympus) was used to capture images.

2.8. Flow cytometry analysis

Annexin V-PI double staining kit (BD Biosciences, USA) was adopted to measure CAL-27 and SCC-9 cell apoptosis. Briefly, transfected cells were treated with centrifugation followed by staining with binding buffer. Cell apoptotic rate was analyzed using a FACScan flow cytometry (BD Biosciences, USA) and CellQuest software (BD Biosciences).

2.9. Western blotting

Radio-immunoprecipitation assay lysis buffer (Santa Cruz Biotechnology, China) and a bicinchoninic acid kit (Qiagen, Germany) were adopted for protein extraction and concentration determination, respectively. Then, after separated by SDS-PAGE, protein samples were transferred onto a PVDF membrane (Millipore, USA). The membrane first sealed with 5% skim milk powder for 1 h at 25°C followed by incubation with primary antibodies (Abcam, USA) against ZFP36 (ab119779, 1/2000), PCNA (ab18197, 1/1000), Ki67 (ab16667, 1/1000), Bax (ab32503, 1/2000), Bcl-2 (ab182858, 1/2000) and loading control β-actin (ab8226, 1/1000) overnight at 4°C and corresponding secondary antibodies for 1 h at 25°C. Efficient chemiluminescence detection kit (Proandy, China) and ImageJ software (NIH, USA) were respectively adopted to visualize the signals and analyze the intensity of signals.

2.10. Bioinformatics analysis

ENCORI website was adopted to predict PCBP1-AS1 or ZFP36 level in HNSC tissue samples or normal samples [24], downstream miRNAs that share binding area with PCBP1-AS1, and targets of miR-34c-5p.

2.11. RNA immunoprecipitation (RIP) assay

The Magna RIP™ RNA-Binding Protein Immunoprecipitation Kit (Millipore, USA) was used for this assay. After OSCC cells were lysed using RIP lysis buffer (Thermo Fisher Scientifc, USA), the lysate was incubated with the magnetic beads (Invitrogen, USA) conjugated with anti-Ago2 antibody or anti-IgG antibody for 8 h at 4°C. Next, the complex was purified conforming to the manufacturer's protocol. The enrichment of RNAs was examined via RT-qPCR.

2.12. Luciferase reporter assay

Wild-type or mutated ZFP36 3'UTR containing miR-34c-5p binding area was respectively subcloned into pmirGLO luciferase reporter vectors (Promega, USA) to generate pmirGLO-ZFP36-Wt/Mut. Similarly, miR-34c-5p-Wt/Mut sequence was subcloned to pmirGLO vector to generate pmirGLO-miR-34c-5p-Wt/Mut. Afterwards, pmirGLO-miR-34c-5p-Wt/Mut was cotransfected with

pCDH-PCBP1-AS1 vector or control pCDH vector into OSCC cells, and pmirGLO-ZFP36-Wt/Mut was cotransfected with NC inhibitor, miR-34c-5p inhibitor, or si-PCBP1-AS1#1 into OSCC cells utilizing Lipofectamine 3000 reagent (Invitrogen, USA). Luciferase activities was examined utilizing a Dual-luciferase reporter assay system after 48 h.

2.13. RNA pulldown assay

Biotinylated miR-34c-5p WT/MUT and the negative control (Bio-NC) purchased from Sangon (Shanghai, China) were transfected into OSCC cells for 24 h. Then, cells were lysed, and the lysate was incubated with Dynabeads M-280 Streptavidin (Invitrogen, USA) for 15 min. After RNA was eluted from beads, PCR analysis was performed to examine RNA level.

2.14. Statistical analysis

Data are expressed as the mean ± standard deviation (SD) and were analyzed utilizing SPSS 19.0 (IBM, USA). Significance between two or more groups was analyzed using two-tailed unpaired Student's *t*-test or ANOVA followed by Tukey's *post hoc* analysis. Values of p less than 0.05 were regarded to be statistically significant.

3. Results

3.1. PCBP1-AS1 is downregulated in OSCC cells

According to the bioinformatics analysis from ENCORI, PCBP1-AS1 displayed low expression in HNSC tissues (n=502) compared to that in healthy samples (n=44) (Fig. 1A). Then, PCR was conducted to detect PCBP1-AS1 expression in OSCC cell lines (SCC-9, CAL-27, SCC-15) and healthy oral epithelial cell line NHOK. Consistent with the bioinformatics analysis, qPCR analysis exhibited low PCBP1-AS1 level in OSCC cell lines (Fig. 1B). Moreover, low PCBP1-AS1 level was related to poor prognosis in patients with HNSC according to the analysis from ENCORI website (Fig. 1C).

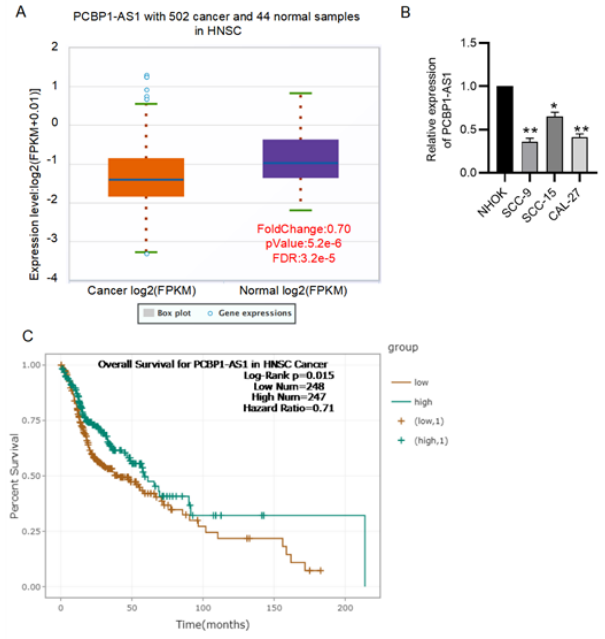

Fig. 1. PCBP1-AS1 is downregulated in OSCC cells. (A) PCBP1-AS1 level in HNSC samples (n=502) and normal samples (n=44) was predicted with ENCORI. (B) Expression of PCBP1-AS1 in OSCC cell lines (SCC-15, CAL-27, and SCC-9) was detected by qPCR. (C) The correlation of PCBP1-AS1 expression and the outcome of patients with HNSC was analyzed with ENCORI website. **p<0.01, *p<0.05.

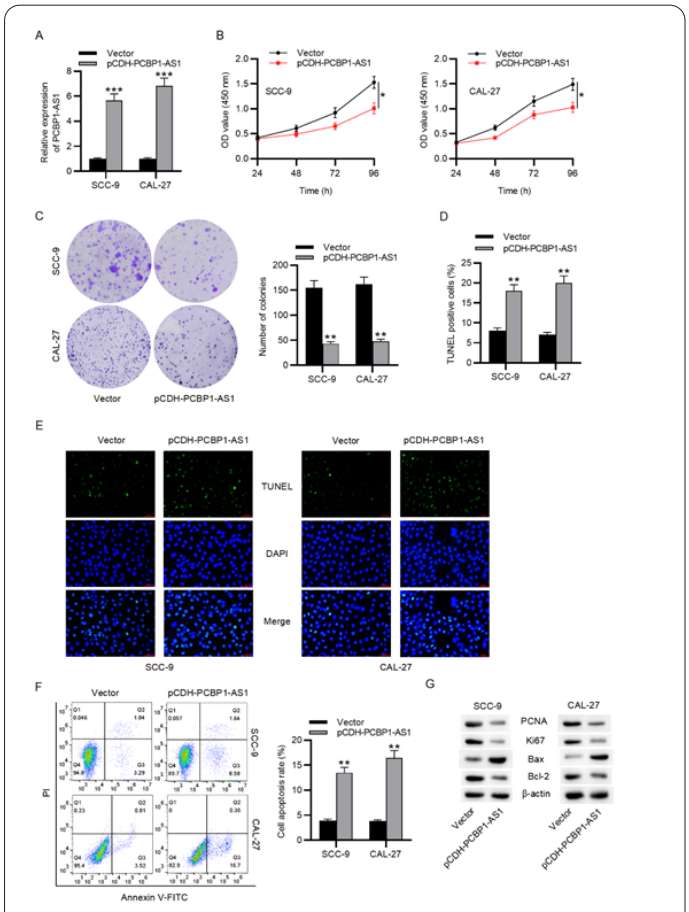

Fig. 2. PCBP1-AS1 overexpression obstructs OSCC cell growth. (A) RT-qPCR analysis of PCBP1-AS1 level in OSCC cells transfected with pCDH vector or pCDH-PCBP1-AS1 vector. (B-C) OSCC cell viability and proliferation in pCDH-PCBP1-AS1 group and control vector group were evaluated utilizing CCK-8 and colony forming assays. (D-F) OSCC cell apoptosis in pCDH-PCBP1-AS1 group and control vector group was measured using TUNEL assays and flow cytometry analyses. (G) Western blotting was conducted to detect protein levels of PCNA and Ki67 (proliferative markers) as well as Bax and Bcl-2 (apoptotic markers) in OSCC cells with pCDH vector transfection. ***p<0.001, **p<0.01, *p<0.05.

3.2. PCBP1-AS1 overexpression inhibits OSCC cell proliferation and enhances cell apoptosis

Gain-of-function experiments were carried out to investigate the functions of PCBP1-AS1 in OSCC cells. PCBP1-AS1 was overexpressed in SCC-9 and CAL-27 cells transfected with pCDH-PCBP1-AS1 as shown by Fig. 2A. In the context of PCBP1-AS1 overexpression, OSCC cell viability was greatly suppressed according to CCK-8 assays (Fig. 2B). In addition, colony forming assays verified that the proliferative capability of OSCC cells in pCDH-PCBP1-AS1 group was also inhibited (Fig. 2C). As evidenced by TUNEL assays and flow cytometry analyses, the number of apoptotic cells was markedly elevated after PCBP1-AS1 overexpression (Fig. 2D-F). Western blotting was conducted to quantify protein expression of proliferative markers (PCNA and Ki67) and apoptotic markers (Bax and Bcl-2). In OSCC cells overexpressing

PCBP1-AS1, reduced PCNA, Ki67 and Bcl-2 levels and increased Bax protein level were discovered (Fig. 2G).

3.3. PCBP1-AS1 interacts with miR-34c-5p in OSCC

Subsequent experiments were carried out to validate the ceRNA hypothesis mediated by PCBP1-AS1 in OSCC. First, subcellular fractionation assay was conducted to identify the dislocation of PCBP1-AS1 in OSCC cells. Fig. 3A showed that PCBP1-AS1 majorly localized in the cytoplasm, validating the post-transcriptional role of PCBP1-AS1 in OSCC. ENCORI website was adopted to seek miRNAs that have binding areas with PCBP1-AS1, and the first five miRNAs were selected and subjected to RT-PCR analysis. As shown by Fig. 3B, miR-34c-5p level was greatly inhibited by overexpressed PCBP1-AS1 in OSCC cells. Additionally, the expression of other miRNAs was not significantly affected by the alternation of PCBP1-AS1 expression (Fig. 3B). Afterwards, the binding ability of PCBP1-AS1 to miR-34c-5p was investigated. The binding area of PCBP1-AS1 and miR-34c-5p was obtained using the bioinformatics tool ENCORI, and the mutant sequence of miR-34c-5p was provided in Fig. 3C. It was indicated that overexpressed PCBP1-AS1 reduced

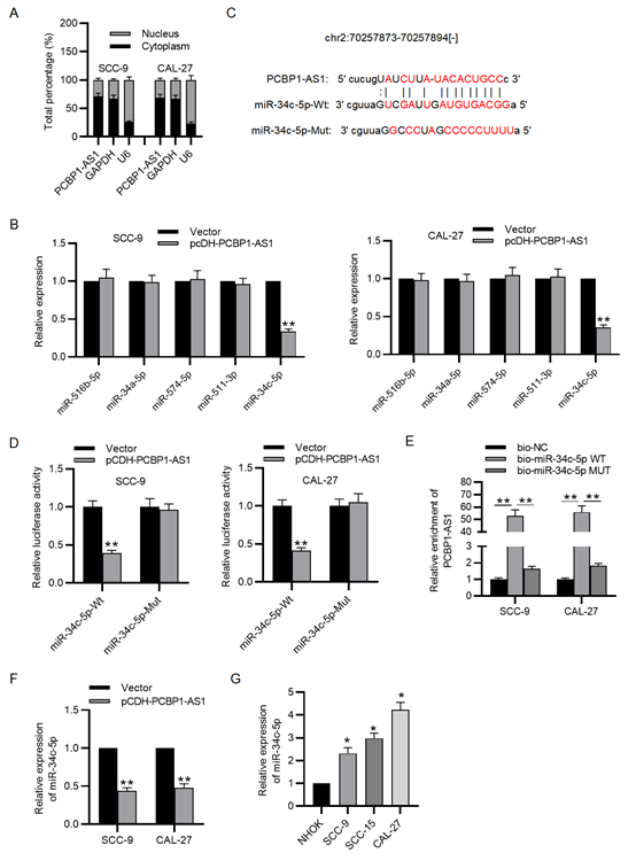

Fig. 3. PCBP1-AS1 bound to miR-34c-5p in OSCC. (A) PCBP1-AS1 location in OSCC cells was determined using a cellular RNA fractionation assay. (B) The impact of PCBP1-AS1 overexpression on expression levels of candidate miRNAs was explored using PCR analysis. (C) The binding area of PBP1-AS1 and miR-34c-5p was obtained at the ENCORI website. (D-E) Luciferase reporter assays and RNA pulldown assays were performed to investigate the binding capacity of PCBP1-AS1 and miR-34c-5p. (F) PCR analysis of miR-34c-5p level in OSCC cells amplifying PCBP1-AS1. (G) miR-34c-5p expression in OSCC cell lines and the control NHOK cell line were subjected to PCR. $^{**}p<0.01$, $^{*}p<0.05$.

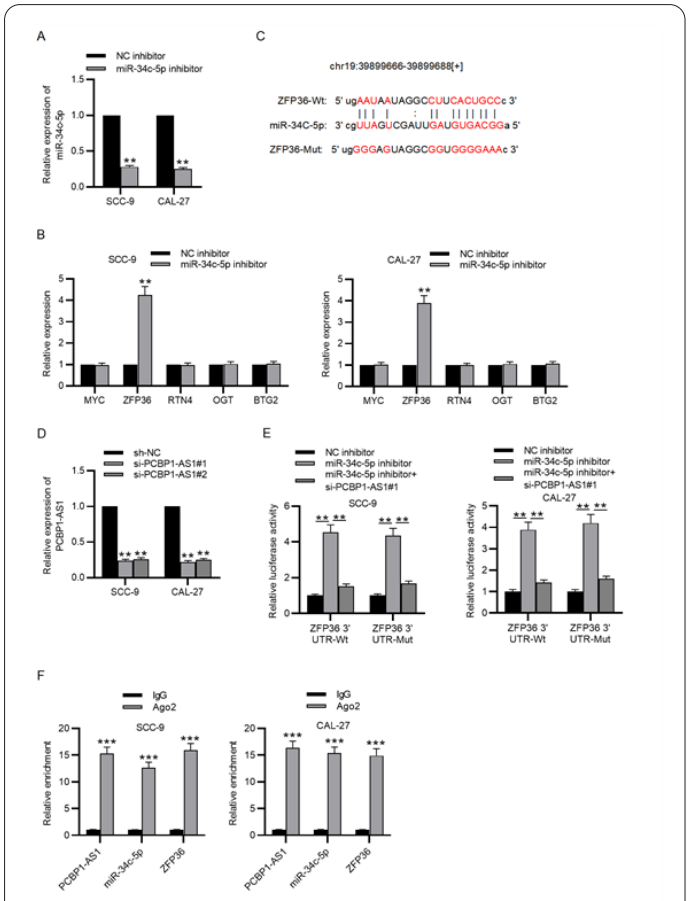

Fig. 4. miR-34c-5p targets ZFP36 3'UTR in OSCC cells. ENCORI website was used to seek the targets of miR-34c-5p, and the top five genes with high binding score were identified. (A) Knockdown efficiency of miR-34c-5p inhibitor was probed using PCR. (B) After miR-34c-5p depletion, the expression of targets was measured utilizing PCR. (C) The binding site of hsa-34c-5p on ZFP36 was predicted with ENCORI. (D) The knockdown efficacy of PCBP1-AS1 in OSCC cells was evaluated through PCR analysis. (E-F) Luciferase reporter and RNA immunoprecipitation assays were carried out to identify the regulatory relationship of PCBP1-AS1, miR-34c-5p and ZFP36. $^{***}p<0.001$, $^{**}p<0.01$.

the luciferase activity of pmirGLO vectors containing miR-34c-5p-Wt while PCBP1-AS1 amplification could not significantly influence the luciferase activity of vectors containing miR-34c-5p-Mut (Fig. 3D). The results demonstrated the binding relation of PCBP1-AS1 and miR-34c-5p in OSCC cells. In addition, PCBP1-AS1 was pulled down by biotinylated miR-34c-5p in cancer cells (Fig. 3E), which further confirmed the binding between the two players. Moreover, PCR analysis revealed that overexpressed PCBP1-AS1 decreased miR-34c-5p expression in OSCC cells (Fig. 3F). Additionally, miR-34c-5p level was increased in SCC-9, SCC-15, and CAL-27 cells compared to that in NHOK cells (Fig. 3G).

3.4. miR-34c-5p targets ZFP36 3'UTR in OSCC cells

The starBase website was used to seek targets of miR-34c-5p, and the top five genes with high Prediction Score were identified. To investigate the impact of miR-34c-5p on these genes, miR-34c-5p inhibitors were used to knock down its expression. PCR analysis showed that miR-34c-5p level was successfully reduced in SCC-9 and CAL-27 cells (Fig. 4A). Among target genes, only ZFP36 was

upregulated in OSCC cells silencing miR-34c-5p (Fig. 4B). The binding area for hsa-miR-34c-5p and ZFP36 was identified using starBase and shown in Fig. 4C. In addition, PCBP1-AS1 was knocked down through transfection of si-PCBP1-AS1 into OSCC cells (Fig. 4D). The luciferase activity of ZFP36 3'UTR-Wt was upregulated in OSCC cells in the context of miR-34c-5p depletion, and the increase in luciferase activity mediated by miR-34c-5p inhibitor was countervailed by PCBP1-AS1 knockdown (Fig. 4E). The regulatory relationship of PCBP1-AS1, miR-34c-5p, and ZFP36 was also verified using RIP assays. We discovered that PCBP1-AS1, miR-34c-5p and ZFP36 were markedly enriched in the antibody Ago2 group compared to those in antibody IgG group of cancer cells (Fig. 4F).

3.5. ZFP36 was upregulated in OSCC cells and correlated with PCBP1-AS1 and miR-34c-5p expression

miR-34c-5p expression was effectively amplified in OSCC cells after miR-34c-5p mimics transfection (Fig. 5A). In the context of miR-34c-5p overexpression, ZFP36 mRNA level was markedly decreased (Fig. 5B). Additionally, the decrease in ZFP36 expression mediated by miR-34c-5p overexpression was elevated by amplified PCBP1-AS1 (Fig. 5B, left panel). In contrast, ZFP36 mRNA level was elevated in the context of miR-34c-5p silencing and then offset by PCBP1-AS1 knockdown (Fig. 5B, right panel). Similarly, ZFP36 protein level was also decreased by miR-34c-5p amplification and then rescued by PCBP1-AS1 upregulation, while ZFP36 protein level was upregulated after miR-34c-5p inhibition and then countervailed by PCBP1-AS1 deficiency (Fig. 5C). According to the bioinformatics tool starBase, ZFP36 was downregulated in HNSC tissue samples (Fig. 5D). The PCR analysis demonstrated that ZFP36 was downregulated in OSCC cells relative to that in oral epithelial cells (Fig. 5E).

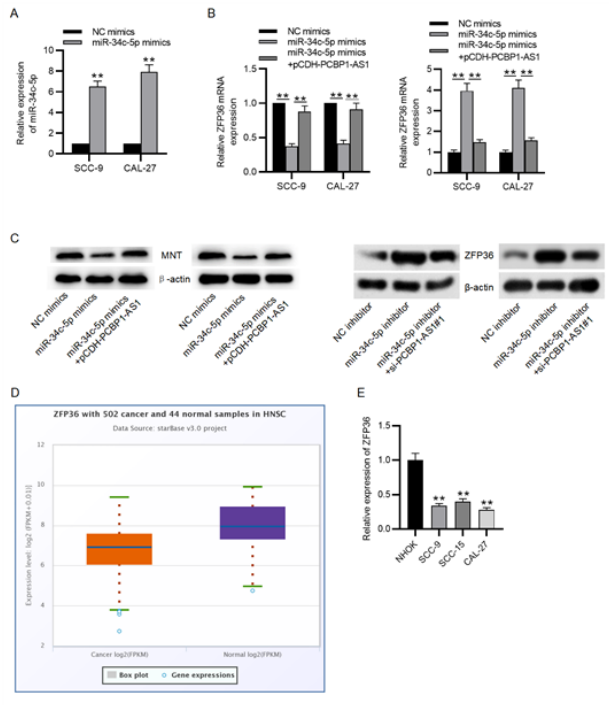

Fig. 5. High ZFP36 expression in OSCC cells and its correlation with PCBP1-AS1 and miR-34c-5p expression. (A) Overexpressing efficacy of miR-34c-5p mimics in SCC-9 and CAL-27 cells was evaluated using qPCR. (B) ZFP36 expression in SCC-9 and CAL-27 cells in response to miR-34c-5p and PCBP1-AS1 overexpression (left panel) or knockdown (right panel) were subjected to qPCR. (C) Western blotting of ZFP36 protein level in OSCC cells in the context of miR-34c-5p and PCBP1-AS1 overexpression (left panel) or silencing (right panel). (D) ZFP36 expression in HNSC samples and normal samples were analyzed using ENCORI. (E) ZFP36 expression in OSCC cells and control NHOK cells were subjected to qPCR. $^{**}p<0.01$.

3.6. ZFP36 silencing abrogates the impacts of PCBP1-AS1 overexpression on OSCC cell growth

ZFP36 protein and mRNA levels were reduced in OSCC cells after si-ZFP36 transfection according to western blotting and PCR (Fig. 6A-B). The repressive impact of PCBP1-AS1 upregulation on the number of viable and proliferative cells could be countervailed by ZFP36 deficiency (Fig. 6C-D). TUNEL assays and flow cytometry analyses indicated that PCBP1-AS1 enhanced the apoptosis of OSCC cells while si-ZFP36 abolished the promoting effect (Fig. 6E-G). As suggested by western blotting, PCNA, Ki67 and Bcl-2 protein level reduced by PCBP1-AS1 overexpression was rescued after the silencing of ZFP36 while Bax protein level was enhanced by PCBP1-AS1 and then partially reversed by ZFP36 deficiency (Fig. 6H).

4. Discussion

Accumulating data indicated that lncRNA exerts critical functions in OSCC tumorigenesis and progression and have potential clinical values [25]. Herein, overexpressed PCBP1-AS1 was discovered to inhibit OSCC cell growth and enhance cell apoptosis. In addition, PCBP1-AS1 was validated to interact with miR-34c-5p and thereby upregulate mRNA ZFP36.

miRNAs are regarded as useful disease biomarkers because of their robust presence in tissues and fluids and their impact on gene expression [26]. Typically, miRNAs affect mRNA stability by binding to 3'UTR of mRNAs [26, 27]. In the ceRNA hypothesis, lncRNAs serve as ceRNAs to interact with miRNAs, thereby protecting mRNAs from degradation [25]. miR-34c-5p exerts tumor-suppressive or oncogenic role in cancer progression. For instance, miR-34c-5p contributes to the eradication of acute myeloid leukemia stem cells via selectively targeting RAB27B [28]. miR-34c-5p facilitates cell proliferation in colon cancer by targeting SIRT6 to activate JAK2/STAT3 signaling pathway [29]. Moreover, miR-34c-5p promotes OSCC malignant behaviors by targeting TRIM29 [30]. In our work, miR-34c-5p was upregulated in OSCC cells, and PCBP1-AS1 bound to miR-34c-5p and suppress miR-34c-5p expression. miR-34c-5p targeted ZFP36 3'UTR to reduce ZFP36 expression.

The functions of ZFP36 in suppressing tumorigenesis and cellular behaviors have been increasingly reported. For example, miR-423 targets ZFP36 to trigger the activation of Wnt and beta-catenin signaling in breast cancer, thus promoting cell growth and migration [31]. ZFP36 is implicated in the ceRNA network mediated by circular RNA 000554, and the circRNA_00554/miR-182/ZFP36 axis inhibits epithelial-mesenchymal transition in breast cancer [32]. Consistent with previous reports, ZFP36 was downregulated in OSCC cells in the present work, and ZFP36 level was positively regulated by PCBP1-AS1. miR-34c-5p targeted ZFP36 3'UTR and repress ZFP36 expression. Silencing ZFP36 offset the impacts of PCBP1-

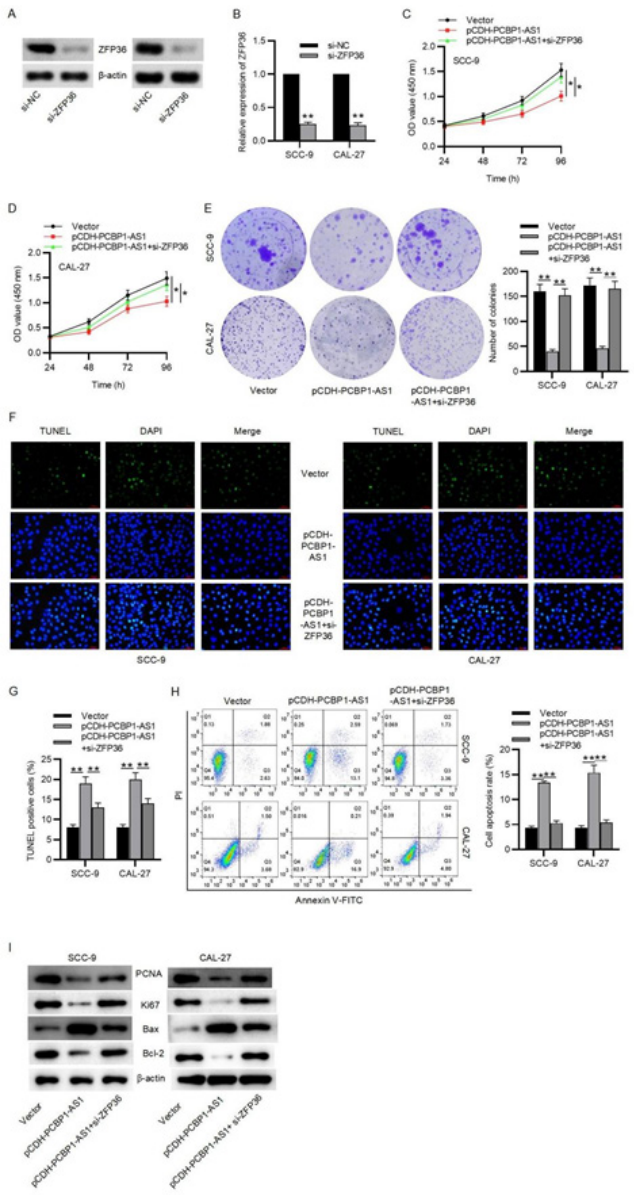

Fig. 6. ZFP36 silencing abrogates the impacts of PCBP1-AS1 overexpression on OSCC cell growth. (A-B) Western blotting and PCR for quantifying ZFP36 levels in cancer cells after transfection of si-ZFP36. (C-D) OSCC cell viability and proliferation in control vector group, pCDH-PCBP1-AS1 vector group, and pCDH-PCBP1-AS1 + si-ZFP36 group were examined through CCK-8 and colony forming assays. (E-G) TUNEL assay and flow cytometry analysis were performed to probe OSCC cell apoptosis in above three groups. (H) Western blotting of protein levels of PCNA and Ki67 (proliferative markers) and apoptosis markers (Bax and Bcl-2) in OSCC cells. *p<0.05, **p<0.01.

AS1 on OSCC cell growth.

In conclusion, PCBP1-AS1 inhibits OSCC cell growth by serving as a ceRNA against miR-34c-5p to regulate ZFP36 expression. The study helps to understand the cellular biological basis of OSCC progression and might provide novel therapeutic targets for OSCC patients in the future.

Informed Consent

The authors report no conflict of interest.

Availability of data and material

We declared that we embedded all data in the manuscript.

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