INTRODUCTION

Recently, surging evidence indicated that dysfunction of lncRNA was involved in human cancer. Wang et al. testified that serum long non-coding RNAs HOX transcript antisense intergenic RNA (LNCRNA HOTAIR) could be used as a potential biomarker for the diagnosis of oesophageal squamous cell carcinoma. Overexpression of IncRNA PVT1 Oncogene (PVT1) promoted proliferation of non-small cell lung cancer (NSCLC) cells by interaction with Enhancer of zeste homolog 2 (EZH2), thereby inhibiting the expression of large tumour
suppressor kinase 2 (LATS2). The overexpression of FEZF1-AS1 was found in colorectal cancer (CRC), which is a newly discovered carcinogenic lncRNA in human digestive tract cancer.

SRY-related HMG-box 4 (SOX4) is a potent tumour suppressor gene, and its expression is induced in many types of cancer. Castro-Oropeza et al demonstrated that LncRNA DANCR competed with Sox4 mRNA to bind with miR-138, thereby affecting the expression of Sox4. Sun et al found that miR-339-5p directly targeted SOX4 and exerted anti-proliferative effects in acute myeloid leukaemia (AML). Yang et al found that IncRNA ARNILA acted as a competitive endogenous RNA to promote SOX4 by supporting mir-204 in triple-negative breast cancer. In addition, SOX4 was involved in the regulation of EMT processes in carcinogenesis of liver, colon, prostate and breast tissues. LncRNA FEZF1-AS1 was a novel oncogene discovered recently. However, the expression levels of SOX4 in epithelial ovarian cancer (EOC) and its correlation with FEZF1-AS1 have rarely been reported. In this study, our results for the first time revealed that by up-regulating SOX4, FEZF1-AS1 interacted with miR-130a-5p to accelerate metastasis and proliferation of EOC cells.

2 | METHODS

2.1 | Clinical samples

Fifty-two paired EOC specimens, serum samples and surrounding normal tissues were taken from individuals who underwent tumour surgeries in China-Japan Union Hospital of Jilin University from January 2012 to October 2014 were retrospectively studied. All clinical tissues were confirmed by experienced pathologists who confirmed the diagnosis of EOC samples. None of the enrolled individuals had chemotherapy or radiotherapy preoperatively. EOC tissue samples were obtained and then immediately frozen in liquid nitrogen at -80°C until analysis. All samples were diagnosed in accordance with the World Health Organization criteria. The investigation was agreed by the Clinical Research Ethics Committee of the China-Japan Union Hospital of Jilin University, and the informed consent and written agreements were received from patients. The clinicopathological parameters were illustrated in Table 1.

2.2 | Cell lines

EOC cell lines PEO1, SKOV-3, COC1, CAOV3, A2780, 3AO and human normal ovarian epithelial cell lines (IOSE-80) were purchased from the American Type Culture Collection (ATCC). The cells were cultured in RPMI 1640 medium supplemented with 10% FBS (ExCell Bio), 100 mg/mL streptomycin and 100 U/mL penicillin (Gibco; Thermo Fisher Scientific, Inc) and maintained in an incubator at 37°C with 5% CO₂.

2.3 | Luciferase reporter assay

About 2 × 10⁵/well OC cells were seeded in 24-well plates. Cells were cotransfected with FEZF1-AS1-3′-UTR WT or mutant vector along with miR-130a-5p mimics/inhibitor, and pRL-SV40 renilla plasmid (Promega Corporation) using Lipofectamine 2000. After 48 hours, the dual-luciferase reporter assay system (Promega) with the luminometer (Promega) was used to measure the activities of firefly and renilla luciferase. Each treatment was performed in triplicate.

2.4 | MTT assay

The cells were seeded into 96-well plates at a density of 1 × 10³ cells per well with DMEM medium containing 10% FBS for 24 hours, and 5 μg/mL (10 μL) MTT was supplemented into each well, which were then incubated for 4 hours away from the light. Next, 150 μL dimethylsulphoxide was added into the wells, which was then measured at the optical density (OD) of 570 nm.

2.5 | Cell colony formation assay

We inoculated cells in 6-well plates with DMEM medium supplemented with 10% FBS for 14 days. Next, at room temperature, colonies were fixed with methanol for 20 minutes, which were then stained with 0.1% crystal violet for 10 minutes (Invitrogen). The number of observed colonies was counted under an inverted microscope.

2.6 | Cell apoptosis analysis

COC1, SKOV-3 and PEO1 cells transfected with si-NC or si-FEZF1-AS1 were collected and subjected to double staining with FITC-Annexin V and PI using Apoptosis Detection Kit (CWBIO).

2.7 | Cell invasion and migration assays

Cell invasion and migration assays were conducted with Boyden Transwell chambers (BD Biosciences) as previously described.

2.8 | Wound healing assay

SKOV-3, COC1 as well as PEO1 cells were treated with si-FEZF1-AS1 or si-NC transfection in DMEM medium with 10% FBS, which was kept for 48 hours with 5% CO₂ at 37°C. Linear scratches were created on the cell layer with a pipette tip, and the cells were kept for 24 hours in DMEM medium free of serum. Wound healing process
was observed with optical microscope and then analysis was performed with Image J software.

### 2.9 qRT-PCR assay

Total RNAs were extracted from EOC cells and tissues of patients. A total of 10 ng total RNA was reverse-transcribed into cDNAs using Reverse Transcription Kit (Takara). SYBR Green Real-time PCR Master Mix was applied, and reagents were incubated at 95°C for 1 minute, which were subjected to 40 cycles of 95°C for 10 seconds, 58°C for 15 seconds and 72°C for 1 minute. The primers of miR-218, miR-142, miR-193a, miR-130a-5p and miR-499 were obtained from TransGen Biotech, Shanghai, China. U6 small nuclear RNA: 5′-GAGAAGGGCTATCCAGGAAG-3′ (forward), 5′-CCGAAAGGAATTGAAGCACT-3′ (reverse) was used as the internal standard. The primers for FEZF1-AS1: 5′-ACACA TTACCAAACCAGC-3′ (forward), 5′-GGTCCAGGCCCCATTTATT-3′ (reverse). SOX4: 5′-ACAGTTTTGTGCCCCTCA-3′ (forward) and 5′-GGGTGATGCTGTGTTTTG-3′ (reverse); Slug: 5′-CACGATCAGCTCCGCTCA-3′ (forward) and 5′-GCCAGACCCAATACC-3′ (reverse). GAPDH was used as the internal control. The expression was calculated by the 2−ΔΔCt method.

### 2.10 Western blot assay

Protein (60 μg) was separated using 10% SDS-PAGE, which was then transferred onto PVDF membranes. Then, the membranes were blocked with 5% (w/v) non-fat milk. After blocking, the membranes were incubated with monoclonal primary antibody against vimentin (sc-51721, 1:800; Santa Cruz, CA, USA), E-cadherin (ab15148, 1:800; Abcam), Slug (ab27568, 1:600; Abcam), SOX4 (1:800; Abcam), N-cadherin (sc-59987, 1:1000; Santa Cruz) and anti-GAPDH (ab14247, 1:2000; Abcam) at 4°C overnight. After incubating with secondary antibodies (Sigma) at room temperature for 60 minutes, protein bands were detected with the gel image system (Bio-Rad).

### 2.11 RNA immunoprecipitation (RIP) assay

As previously described, Magna RIP RNA-Binding Protein Immunoprecipitation Kit was applied (Millipore) to perform RNA immunoprecipitation (RIP) assays. Cell extracts were incubated with antibodies against Ago2 (Cell Signaling). Normal mouse IgG was regarded as negative control.

### 2.12 Immunofluorescent staining assay

Blocking buffer (5% normal goat serum, 0.1% Triton-X 100 in PBS and 3% bovine serum albumin) was used to incubate EOC cells for 60 minutes. Anti-SOX4 antibody (1:500; Abcam), Anti-vimentin antibodies (1:200; Abcam), Anti-PCNA antibody (1:500; Abcam), Anti-E-cadherin antibody (1:200; Abcam) and Anti-Slug antibody (1:150; Abcam) were then used to incubate the cells overnight. PBST was used to wash cells for three times for 5 minutes, and secondary antibodies (Invitrogen) were used to incubate cells at room temperature for 2 hours. DAPI was used to counterstain cell nuclei (Burlingame, CA). We applied a Nikon Ti inverted fluorescence microscope to acquire photos.

### 2.13 Statistical analysis

SPSS 21.0 software was used to perform analysis on statistical variations. Experimental results were shown as mean ± SD. One-way ANOVA or Student’s t test was applied to conduct

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**Table 1** Clinicopathological parameters and FEZF1-AS1 expression in EOC patients

| Characteristics         | Total number | FEZF1-AS1 expression |  |  |  |  |  |  |  |  |
|-------------------------|--------------|----------------------|---|---|---|---|---|---|---|---|
|                         |              |                      | High | Low | P-value |  |  |  |  |  |
|                         |              |                      | n (%) | n (%) |          |  |  |  |  |  |
| Age                     |              |                      |  |  |  |  |  |  |  |  |
| <55                     | 27           | 15 (55.6)            | 12 (44.4) | .427 |  |  |  |  |  |  |
| ≥55                     | 25           | 15 (60.0)            | 10 (40.0) |  |  |  |  |  |  |  |
| Differentiation         |              |                      |  |  |  |  |  |  |  |  |
| Well                    | 18           | 9 (50.0)             | 9 (50.0) | .105 |  |  |  |  |  |  |
| Moderate                | 21           | 14 (66.7)            | 7 (33.3) |  |  |  |  |  |  |  |
| Poor                    | 13           | 7 (53.8)             | 6 (46.2) |  |  |  |  |  |  |  |
| Menopause               |              |                      |  |  |  |  |  |  |  |  |
| Pre-                    | 24           | 12 (50.0)            | 12 (50.0) | .178 |  |  |  |  |  |  |
| Post-                   | 28           | 18 (64.3)            | 10 (35.7) |  |  |  |  |  |  |  |
| Depth of invasion       |              |                      |  |  |  |  |  |  |  |  |
| T1-T3                   | 20           | 5 (25.0)             | 15 (75.0) | .004 |  |  |  |  |  |  |
| T4                      | 32           | 25 (78.1)            | 7 (21.9) |  |  |  |  |  |  |  |
| Lymph node metastasis   |              |                      |  |  |  |  |  |  |  |  |
| Absent (NO)             | 18           | 6 (33.3)             | 12 (66.7) | <.001 |  |  |  |  |  |  |
| Present (N1-N3)         | 34           | 24 (70.6)            | 10 (29.4) |  |  |  |  |  |  |  |
| Distant metastasis      |              |                      |  |  |  |  |  |  |  |  |
| Absent (M0)             | 17           | 4 (23.5)             | 13 (76.5) | .021 |  |  |  |  |  |  |
| Present (M1-M3)         | 35           | 26 (74.3)            | 9 (26.7) |  |  |  |  |  |  |  |
| TNM stage               |              |                      |  |  |  |  |  |  |  |  |
| I-II                    | 19           | 4 (21.1)             | 15 (78.9) | <.001 |  |  |  |  |  |  |
| III-IV                  | 33           | 26 (78.8)            | 7 (21.2) |  |  |  |  |  |  |  |
| FIGO Stage              |              |                      |  |  |  |  |  |  |  |  |
| I- II                   | 21           | 16 (76.2)            | 5 (23.8) | .008 |  |  |  |  |  |  |
| III-IV                  | 31           | 14 (45.2)            | 17 (54.8) |  |  |  |  |  |  |  |
comparison of 2 or multiple groups. Correlations were analysed with Pearson's correlation. *P*-value < .05 was deemed to be significant difference.

3 | RESULTS

3.1 FEZF1-AS1 was overexpressed in EOC

FEZF1-AS1 expression in 52 EOC specimens and the para-carcinoma tissues were detected by qRT-PCR. Compared with para-carcinoma tissues, FEZF1-AS1 expression was notably increased in EOC specimens (*P* < .001, Figure 1A). Moreover, serum levels of FEZF1-AS1 were dramatically up-regulated in EOC patients than healthy controls (*P* = .0036, Figure 1B). Most importantly, the expression levels of FEZF1-AS1 in serum were correlated with those in EOC tissues positively (*P* = .001, *r*² = .5273, Figure 1C). Furthermore, overexpressed FEZF1-AS1 was found in EOC cell lines compared with IOSE 80 cell line (Figure 1D).

3.2 Correlation between clinicopathological parameters and the expression of FEZF1-AS1

According to the expression of FEZF1-AS1 detected by qRT-PCR, EOC patients were classified as high (n = 30, > twofold of normal tissues) and low FEZF1-AS1 expression group (n = 22). Patients in high FEZF1-AS1 expression group have worse lymphatic metastasis.

| Variable                | Univariate analysis | Multivariate analysis |
|------------------------|--------------------|----------------------|
|                        | HR                 | 95% CI               | *P*-value | HR                 | 95% CI               | *P*-value |
| Depth of invasion      | 2.023              | 1.903-2.426          | .023      | 2.114              | 1.905-2.403          | .003      |
| Lymph node metastasis  | 1.863              | 1.382-2.054          | .035      | 2.000              | 1.758-2.336          | .022      |
| Distant metastasis     | 1.654              | 1.436-1.732          | .020      | 2.310              | 1.763-2.453          | <.001     |
| TNM stage              | 1.874              | 1.683-2.407          | <.001     | 2.884              | 2.509-3.412          | .014      |
| FEZF1-AS1              | 2.741              | 2.437-3.102          | .001      | 2.884              | 2.509-3.412          | .014      |

**TABLE 2** Univariate and multivariable Cox proportional hazard regression analyses for OS in EOC patients

![FIGURE 1](image-url)
(P < .001), deeper invasion (P = .004), distant metastasis (P = .021), advanced TNM Classification of Malignant Tumours (TNM) stage (P < .001) and FIGO Stage (P = .008). Nevertheless, no significant association was found between FEZF1-AS1 expression level and age, differentiation or menopause (Table 1).

3.3 | Poor prognosis was associated with induced FEZF1-AS1 expression in EOC patients

Kaplan-Meier analysis showed that compared with patients in high FEZF1-AS1 expression group, the 5-year overall survival (OS) was
remarkably higher in low expression of FEZF1-AS1 group (\(P = .005\), Figure 1E). Univariate analysis results demonstrated that invasion depth (\(P = .021\)), lymph node metastasis (\(P = .030\), FEZF1-AS1 expression levels (\(P = .001\)), distant metastasis (\(P = .003\), TNM stage (\(P < .001\)) were closely related to OS (Table 2). Moreover, multivariate analyses showed that the expression of FEZF1-AS1 (\(P = .014\)), depth of invasion (\(P = .003\), TNM stage (\(P < .001\)), and lymph node metastasis (\(P = .022\)) were independent indicators for OS prognosis in EOC patients (Figure 1F). ROC curve analysis found that serum FEZF1-AS1 level distinguished EOC patients from normal controls (AUC = 0.9483, 95% CI: 0.915-0.998, \(P < .001\), Figure 1G). Therefore, FEZF1-AS1 could serve as a critical indicator (cut-off value = 2.41, sensitivity: 87.4%, specificity: 76.2%). In addition, serum FEZF1-AS1 level in post-surgery EOC tissues decreased significantly compared with pre-surgery tissues (\(P < .001\); Figure 1H).

### 3.4 Silencing of FEZF1-AS1 inhibited cell proliferation of EOC cell lines

Three si-FEZF1-AS1s and si-NC were transfected into COC1 and SKOV-3 cells, and qRT-PCR was performed to verify the transfection efficiencies. The transfection of si-FEZF1-AS1-1 and si-FEZF1-AS1-2 had higher interference efficiencies and was used for further experiments (\(P < .01\), Figure 2A). MTT assay showed that compared with si-NC group, cell proliferative rate was remarkably repressed in groups transfected with si-FEZF1-AS1-1/2 (\(P < .01\), Figure 2B). Colony formation assay showed that relative to si-NC group, cell colony number in groups transfected with si-FEZF1-AS1-1/2 was obviously lower (\(P < .05\), Figure 2C). Flow cytometric analysis manifested that by comparison to si-NC group, the cell apoptotic rate in si-FEZF1-AS1-1/2 groups was significantly higher (\(P < .05\), Figure 2D). Moreover, the expressions of apoptotic related genes were increased after FEZF1-AS1 knock-down (Figure 2E). Together, silencing of FEZF1-AS1 promoted cell apoptosis and repressed cell proliferation in EOC cells.

### 3.5 Silencing of FEZF1-AS1 hindered cell invasion and migration in EOC cells

Transwell assay results suggested that silencing of FEZF1-AS1 hindered the cell migration and invasion of SKOV-3, COC1 and PEO1 cells in vitro (\(P < .01\), Figure 3A,B). Similarly, wound healing assay showed that compared with si-NC group, reduced cell migration ability was found in COC1, SKOV-3 and PEO1 cells after silencing FEZF1-AS1 (\(P < .01\), Figure 3C,D).

### 3.6 The scanning and certification of candidate miRNAs

The candidate miRNAs which could directly bind to FEZF1-AS1 were indentified with online bioinformatics instruments, miRcode (http://www.mircode.org/) and Targetscan (http://www.targetscan.org/vert_72/). It was showed that the miR-130a-5p expression was the most up-regulated by FEZF1-AS1 knock-down among the candidate miRNAs (Figure 4A; \(P < .01\)). To verify the binding site of FEZF1-AS1 to miR-130a-5p, wt-FEZF1-AS1 and mut-FEZF1-AS1 3′-UTR luciferase reporter vector were constructed and transfected into the SKOV-3 cell (Figure 4B). Luciferase activity results showed that...
wt-FEZF1-AS1 3′-UTR was dramatically attenuated via being transfected with miR-130a-5p-mimic and notably increased by transfecting with miR-130a-5p-inhibitor (P < .01). Nevertheless, no significant difference of mut-FEZF1-AS1 reporter was shown in miR-130a-5p-inhibitor nor miR-130a-5p-mimics transfected groups (P < .01).

3.7 Correlation of miR-130a-5p and FEZF1-AS1 in EOC cells

qRT-PCR result indicated that compared with the group transfected with si-NC, the expression of miR-130a-5p was dramatically increased after silencing FEZF1-AS1 (Figure 4C; P < .01). Also, the expression of FEZF1-AS1 mRNA was notably attenuated by miR-130a-5p overexpression while increased by miR-130a-5p suppression (P < .01, Figure 4D). Inhibitory effect of si-FEZF1-AS1 on EOC cell growth was partly restored by miR-130a-5p knock-down (Figure 4E,F; P < .01). Similar effect was detected in cell MTT assay (Figure 4G,H; P < .01). Therefore, it was concluded that FEZF1-AS1 might induce carcinogenesis and growth via inhibiting the activity of miR-130a-5p in EOC.

3.8 SOX4 accelerated EOC cell progression

Compared with surrounding healthy tissues, SOX4 expression was notably promoted in EOC tissues (Figure 5A,B; P < .01).
Additionally, SOX4 expression level was dramatically decreased by FEZF1-AS1 knock-down in vitro (P < .01, Figure 5C,D).

Furthermore, compared with si-NC group, the immunofluorescence of SOX4 staining was attenuated by FEZF1-AS1 knock-down (P < .01; Figure 5E,F). FEZF1-AS1 mRNA expression was obviously reduced by silencing SOX4 in EOC cell lines (P < .01; Figure 5G). We transfected the plasmids of cDNA (pcDNA)-3.1/SOX4 into EOC cell lines (Figure 5H; P < .01). MTT assay revealed that the cell proliferation of EOC cells was significantly attenuated by FEZF1-AS1 knock-down and was increased by SOX4 overexpression. However, these inhibitory effects were partly restored by SOX4 overexpression (P < .01; Figure 5I). Taken together, FEZF1-AS1 modulated cell proliferation of EOC cells through targeting SOX4.
3.9 | FEZF1-AS1 acted as a ceRNA to miR-130a-5p through targeting SOX4

The wt-SOX4 or mut-SOX4′-UTR luciferase reporter vectors and inhibitor-NC/miR-130a-5p-inhibitor or mimics-NC/miR-130a-5p-mimics were applied to co-treat SKOV-3 cells, separately. Compared with the mimics-NC group, the wt-SOX4 3′UTR vector activity was notably decreased in the miR-130a-5p-mimics group (P < .01, Figure 6A,B). The miR-130a-5p expression was obviously down-regulated in EOC tissue samples relative to that in the adjacent normal tissue (Figure 6C, P < .01). In addition, SOX4 expression was decreased by miR-130a-5p overexpression and increased by miR-130a-5p suppression in EOC cell lines (Figure 6D-G, P < .01). The expression of SOX4 protein was decreased by si-FEZF1-AS1
transfection, but up-regulated by miR-130a-5p-inhibitor transfection in EOC cell lines (P < .01, Figure 6H,I).

4 | DISCUSSION

FEZF1-AS1 is located on chromosome 7 on the opposite strand of FEZF1. FEZF1-AS1 acts as an oncogene in gastric cancer by activating Wnt signalling pathway or suppressing p21 expression.\textsuperscript{11,15} The oncogenic roles of FEZF1-AS1 were also observed in colorectal cancer and lung cancer.\textsuperscript{16,17} Also, LncRNA FEZF1-AS1 has been revealed as potential therapeutic target, its expression was significantly associated with the overall survival of patients with hepatocellular carcinoma.\textsuperscript{18} Similarly, in this study, FEZF1-AS1 was found as oncogenic IncRNA, which was significantly increased in both serums and EOC tissues. Kaplan-Meier analysis found that higher FEZF1-AS1 expression was related to adverse clinical pathological parameters as well as poor survival rate, such as lymph node metastasis, higher pathological T stage, invasion and distant metastasis. Furthermore, the present study suggested that serum FEZF1-AS1 level was capable of differentiating EOC patients from the healthy controls. Furthermore, the study revealed that FEZF1-AS1 was promising to be taken as an important diagnostic as well as prognostic predictor for those with EOC. Functional experiments found that silencing of FEZF1-AS1 remarkably suppressed cell colony formation, proliferation, migrative and invasive abilities, whereas enhanced cell apoptosis of EOC. This is for the first time uncovered the function of FEZF1-AS1 expression in EOC patients, potentiating that FEZF1-AS1 promoted tumour formation in EOC metastasis as well as progression.

miR-130a-5p has been indicated to be expressed in different kind of tumours, which played an inhibitory role in modulating cell proliferation and apoptosis of cancer cells. Xian et al\textsuperscript{19} reported that miR-130a-5p regulated CB1R expression through the Wnt/β-catenin signalling pathway. Moreover, Xu et al demonstrated that HOXA11-AS exerted its oncogenic functions in glioma cells by epigenetically suppressing miR-130a-5p.\textsuperscript{20} Consistently, we observed notably increased miR-130a-5p expression after silencing of FEZF1-AS1 in COC1, SKOV-3 and PEO1 cells. Meanwhile, a negative correlation was found between the expression of miR-130a-5p and FEZF1-AS1 in EOC tissues. Furthermore, a luciferase assay detected that FEZF1-AS1 directly bound with miR-130a-5p. miR-130a-5p inhibition reversed the suppressive effects of FEZF1-AS1 knock-down on EOC tumour proliferation as well as distant metastasis. Taken together, FEZF1-AS1 inhibited miR-130a-5p by regulating its downstream targets in EOC.

SOX4, a transcription factor of the member of the Sry-related high mobility group box (Sox) family, was recognized a master mediator in cancer stemness and tumorigenicity.\textsuperscript{21} SOX4 has been revealed to promote tumorigenesis in diverse cancers, including prostate cancer, gastric cancer and liver cancer.\textsuperscript{22-24} A recent study demonstrated that Sox4 was regulated by IncBRM via competitively binding miR-204.\textsuperscript{25} The present study found the overexpression of SOX4 both in EOC cell lines and tissues. Furthermore, expression of SOX4 protein in COC1, SKOV-3 and PEO1 cells was significantly reduced after silencing of the FEZF1-AS1. In addition, the overexpression of SOX4 partially restored the suppressive impact of si-fefz1-as1 on the growth of cells after being cotransfected with si-FEZF1-AS1 and SOX4 overexpression plasmids into EOC cell lines. It was proved that FEZF1-AS1 may regulate the proliferation of EOC cells via modulating SOX4 expression.

The apoptosis rates of EOC cells increased significantly by FEZF1-AS1 knock-down. Besides, the expressions of Bcl-2 family members and cleaved caspase3 were up-regulated by silencing of FEZF1-AS1. For some miRNAs, SOX4 has been identified as a target site. For instance, by targeting SOX4, miR-130a-5p served as a tumour inhibitor in gastric cancer.\textsuperscript{3} Interestingly, in vitro studies showed that SOX4 expression was repressed by overexpression of miR-130a-5p and enhanced by blocking of miR-130a-5p.

miR-130a-5p-5p was verified to directly bind with SOX4 in EOC, and further it was confirmed that FEZF1-AS1 interacted with SOX4 to regulate cell migration, proliferation, and invasion of EOC. Therefore, it could be concluded that FEZF1-AS1 regulated SOX4 via miR-130a-5p. Mechanistic study showed that the suppressive effect of FEZF1-AS1 knock-down on SOX4 expression was partially restored with miR-130a-5p inhibition (Figure 7). All these data further confirmed that FEZF1-AS1 regulated SOX4 through miR-130a-5p. However, there are still several limitations in this study. Even though we showed that knock-down of FEZF1-AS1 significantly inhibited proliferation and invasion of EOC cell lines, whether overexpression of FEZF1-AS1 can enhance those processes remains to be explored. In addition, further studies still needed to explore the functional of FEZF1-AS1 in regulating the progression of EOC in a larger cohort.
CONCLUSIONS

In summary, it was for the first time discovered that the function of FEZF1-AS1 was critical in the tumorigenesis of EOC. This study revealed that FEZF1-AS1/miR-130a-5p/SOX4 axis was involved in tumour metastasis and proliferation of EOC cells, which will facilitate the exploration of novel treatment strategies for EOC.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

LXJ and SZQ designed the experiments; SZQ and GSY performed the experiment, XLL analysed the data; SZQ wrote the paper. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

All data sets generated for this study are included in the manuscript.

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