LncRNA LIFR-AS1 overexpression suppressed the progression of serous ovarian carcinoma

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Abstract
Background: Serous ovarian carcinoma (SOC) is a common malignant tumor in female reproductive system. Long noncoding RNA (lncRNA) LIFR-AS1 is a tumor suppressor gene in colorectal cancer, but its effect and underlying mechanism in SOC are still unclear. Therefore, this study focuses on unveiling the regulatory mechanism of LIFR-AS1 in SOC.

Methods: The relationship between LIFR-AS1 expression and prognosis of SOC patients was analyzed by TCGA database and Starbase, and then, the LIFR-AS1 expression in SOC tissues and cells was detected by quantitative real-time PCR (qRT-PCR) and in situ hybridization (ISH). Besides, the relationship between LIFR-AS1 and clinical characteristics was analyzed. Also, the effects of LIFR-AS1 on the biological behaviors of SOC cells were measured by Cell Counting Kit-8, colony formation, and wound-healing and Transwell assays, respectively. Western blot and qRT-PCR were employed to determine the protein expressions of genes related to proliferation (PCNA), apoptosis (cleaved caspase-3), epithelial-mesenchymal transition (E-cadherin, N-cadherin, and Snail).

Results: LIFR-AS1 was lowly expressed in SOC, which was correlated with the poor prognosis of SOC patients. Low expression of LIFR-AS1 in SOC was associated with the tumor size, clinical stage, lymph node metastasis, and distant metastasis. LIFR-AS1 overexpression promoted the expressions of cleaved caspase-3 and E-cadherin while suppressing the malignant behaviors (proliferation, migration, and invasion) of SOC cells, the expressions of PCNA, N-cadherin, and Snail. Besides, silencing LIFR-AS1 exerted the effects opposite to overexpressed LIFR-AS1.

Conclusion: LIFR-AS1 overexpression inhibits biological behaviors of SOC cells, which may be a new therapeutic method.

Keywords
epithelial–mesenchymal transition, LIFR-AS1, proliferation, serous ovarian carcinoma

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Ovarian cancer (OC) is one of the most common malignancies of the female reproductive system, and the WHO estimates that there are approximately 225, 500 newly diagnosed cases of OC and approximately 140, 200 newly emerged deaths worldwide each year. Although the diagnosis and treatment of malignant tumors have gradually improved in recent years, the mortality rate of OC still ranks first in gynecological malignancies. The most common pathological type of OC is epithelial ovarian cancer, 75% of which are serous ovarian carcinomas (SOCs). SOC has been classified into various stages, including ovarian serous cystadenoma, borderline ovarian serous, low-grade SOC, and high-grade SOC, with different expressions of specific tumor markers at various stages. SOC lacks a reliable early diagnostic indicator and typical early symptoms. Several recent studies have discovered that IncRNAs have powerful gene regulatory function and participate in a variety of pathophysiological processes, playing vital roles in cancer progression, as well as the progression of SOC. For instance, IncRNA MAGI2-AS3 leads to the tumor suppression of high-grade SOC, and IncRNA CTD-2020K17.1 promotes metastasis and proliferation of SOC cells. In addition, IncRNA NEAT1 facilitates the malignant phenotype of SOC by mediating miR-506. There is also evidence that the mechanism of action of some IncRNAs is dependent on their genomic location (sense, antisense, bidirection, intron, and intergene), particularly the positional relationship with neighboring genes, in which antisense IncRNAs are noncoding RNAs encoded by genes located on the opposite strand of protein-coding genes and often completely or partially complementary to protein-coding genes. A large body of evidence has indicated that antisense IncRNAs are pervasive, abundantly present within cells, and have specific cellular localizations, heralding that such molecules may have important biological implications. However, less attention has been paid to this part, and the specific role of antisense IncRNAs in SOC has not been clearly elucidated. Combined with relevant literature and bioinformatics analysis, our study singled out LIFR-AS1 to unveil its effects on SOC.

LIFR-AS1 is a newly discovered IncRNA and has a strong association with tumor progression, which is transcribed in an antisense fashion from the leukemia inhibitory factor receptor (LIFR) gene. LIFR could regulate cell proliferation, differentiation, and phenotype in various cancers, such as colorectal cancer and breast cancer. Few literatures have indicated that LIFR-AS1 exerts suppressive effects on the initiation and progression of assorted cancers, such as breast cancer, lung cancer, and glioma. Nevertheless, the effect and underlying mechanism of LIFR-AS1 in SOC are still dim, which is the direction of this current study.

### TABLE 1 Clinical characteristics of SOC patients

| Parameters                        | LIFR-AS1 expression | p value |
|-----------------------------------|---------------------|---------|
| Age (years old)                   |                     |         |
| <55                               | Low: 21             | High: 27| 0.158   |
| ≥55                               | Low: 23             | High: 16|         |
| Histological subtype              |                     |         |
| Mucinous                          | Low: 28             | High: 25| 0.599   |
| Serous                            | Low: 16             | High: 18|         |
| Tumor size (cm<sup>3</sup>)       |                     |         |
| <10                               | Low: 12             | High: 21| 0.038   |
| ≥10                               | Low: 32             | High: 22|         |
| Tumor location                    |                     |         |
| Unilateral                        | Low: 30             | High: 26| 0.452   |
| Bilateral                         | Low: 14             | High: 17|         |
| Differentiation                   |                     |         |
| Well and moderate                 | Low: 14             | High: 18| 0.331   |
| Poor                              | Low: 30             | High: 25|         |
| Clinical stage                    |                     |         |
| I/II                              | Low: 13             | High: 27| 0.002   |
| III/IV                            | Low: 31             | High: 16|         |
| Lymph node metastasis             |                     | <0.001  |
| No                                | Low: 10             | High: 29|         |
| Yes                               | Low: 34             | High: 14|         |
| Distant metastasis                |                     |         |
| Absent                            | Low: 27             | High: 36| 0.020   |
| Present                           | Low: 17             | High: 7 |         |
| Recurrence                        |                     |         |
| No                                | Low: 15             | High: 20| 0.238   |
| Yes                               | Low: 29             | High: 23|         |
that patients agreed to provide their tissue for clinical research, and the clinical trial program was reviewed and approved by the Ethics Committee of The Second Affiliated Hospital of Jiaxing University (JXEY-ZFYJ045).

2.2 | Bioinformatics assay

Data on LIFR-AS1 expression in SOC tissues were retrieved from TCGA database (https://www.cancer.gov/about-nci/organization/ccg/research/structural-genomics/tcga), and the relationship between LIFR-AS1 high (n = 187) or low expression (n = 187) and overall survival (150 months) of SOC patients was analyzed by Starbase (http://starbase.sysu.edu.cn/).

2.3 | Cell culture

Human Ovarian Surface Epithelial (HOSE) cells (7310, Yuhengfeng biotech,) were grown in Ovarian Epithelial Cell Medium (OEpiCM, 7311, Yuhengfeng biotech). A2780 cells (CBP60283, Cobioer,) were cultured in RPMI-1640 medium (R0883, Sigma-Aldrich), and the relationship between LIFR-AS1 high (n = 187) or low expression (n = 187) and overall survival (150 months) of SOC patients was analyzed by Starbase (http://starbase.sysu.edu.cn/).

2.4 | In situ hybridization (ISH)

The tissue sections were put into the mixture of 0.8% Pepsin/ Hydrochloric acid solution (EHJ-CAS0164999, JiaHui Biotech,) and digested in a water bath (TSGP28, Thermo Scientific,) at 37°C for 10 min (min). Then tissues were washed with tris-buffered saline (TBS, 28358, Thermo Scientific,) for 3 times (5 min for each time), dehydrated by gradient ethanol, and dried at room temperature.

2.5 | Transfection

The overexpression plasmid of LIFR-AS1 was constructed using pCMV6-Entry vector (PS100001, Origene), and short hairpin RNA targeting LIFR-AS1 (shLIFR-AS1, C02003, 5'-TGGGACTTTGGCAATTACCTAAA-3') were purchased from GenePharma. LIFR-AS1 overexpression plasmid, shLIFR-AS1, and empty vector (negative control) were transfected into the A2780 and SK-OV-3 cells under the help of Lipofectamine 3000 Reagent (L3000001, Thermo Fisher,). Briefly, cells were seeded onto 6-well plates at a density of 3 x 10^5 cells/well until the cells reached 70%–90% confluence. Then, the serum-free medium was utilized to dilute transfection reagent and LIFR-AS1 overexpression plasmid, empty vector, or shLIFR-AS1 to form the reagent/sample mixture, followed by 48 h culture of SOC cells and mixture. The success of transfection was tested by quantitative real-time polymerase chain reaction (qRT-PCR).

2.6 | QRT-PCR

Cell/Tissue Total RNA Isolation Kit (RK02009, Biomarker,) was utilized to isolate the total RNAs, and cDNA synthesis was then operated using RT Master Mix (HY-K0510A, MedChemExpress,). QRT-PCR was utilized for detecting the mRNA expression levels of LIFR-AS1, proliferating cell nuclear antigen (PCNA),

| Gene names | Forward primer (5′-3′) | Reverse primer (5′-3′) |
|------------|----------------------|-----------------------|
| LIFR-AS1   | GCAAAATCTGTGTATATGGTCC | CCGCTTCTTTGTAAGAGGT |
| PCNA       | ACCGCTGCCAGCCGCAATTGTG | AGCTGCAATTTTACCGAGGCTAC |
| E-Cadherin | GGTCTTCTACAGCTACCCAGG | GCTTTCCCTTTGATGACAC |
| N-Cadherin | TGAACACGGCGGGAATGAGG | GCCTACAGTATCTGTTTG |
| Snail      | GACCCACTGATTCTGCAAGAG | CTTGAGGAGCCGACAT |
| GAPDH      | ACCACGATCCATGCACTAC | TCCACCACTTTGCTGTAG |
E-cadherin, N-cadherin, and Snail using SYBR Green Fast qPCR Mix (RK02001, Biomarker.) in a D10 PCR gene amplification instrument (XuSensmart.). PCR conditions were as follows: 40 cycles of denaturation at 95°C for 20 s, annealing at 58°C for 20 s, and extension at 72°C for 20 s. The sequences of the primers are listed in Table 2. Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was chosen as the internal control to normalize the gene expressions using the 2−ΔΔCT method.27

2.7 | Cell counting kit-8 (CCK-8) assay

A2780 and SK-OV-3 cells inoculated on 96-well plates (5 × 10^3 cells/well) were cultured for 24, 48, and 72 h (h) after various treatments, followed by the incubation with CCK-8 reagent (96,992, 10 μl, Sigma-Aldrich, ) for 4 h. The optical density (OD) value was recorded after being washed with Tris-buffered Saline with Tween-20 (TBST; BI-WB025, Sbjbio,) for 30 min. Subsequently, the membranes were incubated with secondary antibodies goat anti-rabbit IgG (1:1000, ab6702, Abcam,) and goat anti-mouse (1:2000, ab150113, Abcam,) at room temperature for 2 h. Next, the membranes were immersed in ECL luminescence reagent (R30199-100 ml, Pierce,) to observe its completion after being developed and photographed in the dark with a GEL-PRO-ANALYZER software (Bethesda,). GAPDH was selected as the internal reference. The primary antibodies involved in this assay mainly comprised those against PCNA (1:1000; Mouse; ab29, Abcam, 29 kDa), E-cadherin (1:1000; Rabbit; ab2302, Abcam, 17 kDa), cleaved caspase-3 (1:500; Rabbit; ab216347, Abcam, 29 kDa), and GAPDH (1:10000; Rabbit; ab181602, Abcam, 36 kDa).

2.8 | Colony formation assay

For the determination of colony formation, 1 × 10^3 SOC cells that suspended in culture media with 10% FBS were placed in 6-well plates, which were subsequently subjected to the incubation at 37 °C with 5% CO_2 for 14 days. Thereafter, the fixation (15 min) and staining (20 min) of A2780 and SK-OV-3 cells were performed with 4% paraformaldehyde (M009, G法人bio,) and 0.5% crystal violet solution (C0121, Beyotime,) followed by being stained with 0.5% crystal violet solution (G1062, Solarbio,) and observed under the microscope (×250).

2.9 | Wound-healing assay

A2780 and SK-OV-3 cells were seeded in a 6-well plate at a density of 5 × 10^3 cells/well until the cells reached 80% confluence. Then, wounds were created every 0.5 cm with a pipette tip. After being rinsed with PBS, the images of wound closure were obtained at 0 and 24 h with the microscope (×100).

2.10 | Transwell assay

The 24-well Transwell chamber (8 μm pores, Corning,) covered with Matrigel (354,234, Corning) was applied in the invasion assay. In brief, SOC cells maintained in serum-free medium (100 μl, 5 × 10^5 cells/mL) were put into the upper chamber, while those cultured in 600 μl medium with 10% FBS were put into the lower chamber. Following the incubation for 24 h, cells on the lower surface of membrane were fixed with 4% paraformaldehyde (BL-G002, Sbjbio,) followed by being stained with 0.5% crystal violet solution (G1062, Solarbio,) and observed under the microscope (×250).

2.11 | Western blot

RIPA lysis buffer (C500007, Sangon,) was applied to extract the total proteins from SOC cells. Following that, the measurement of protein concentration was performed using the BCA kit (E112-01, Vazyme,). Thereafter, 50 μg of total proteins and 5 μl of pre-stained protein marker (MP102-01, Vazyme,) were loaded into the SDS-PAGE gel (P0688, Beyotime,) and then shifted onto the PVDF membranes (FP32, Beyotime,). Later, the membranes were blocked with 5% non-fat milk and cultured with primary antibodies at 4°C overnight, followed by being washed with Tris-buffered Saline with Tween-20 (TBST; BI-WB025, Sbjbio,) for 3 min. Subsequently, the membranes were incubated with secondary antibodies goat anti-rabbit IgG (1:1000, ab6702, Abcam,) and goat anti-mouse (1:2000, ab150113, Abcam,) at room temperature for 2 h. Next, the membranes were immersed in ECL luminescence reagent (R30199-100 ml, Pierce,) to observe its completion after being developed and photographed in the dark with a GEL-PRO-ANALYZER software (Bethesda,). GAPDH was selected as the internal reference. The primary antibodies involved in this assay mainly comprised those against PCNA (1:1000; Mouse; ab29, Abcam, 29 kDa), E-cadherin (1:1000; Rabbit; ab2302, Abcam, 17 kDa), cleaved caspase-3 (1:500; Rabbit; ab216347, Abcam, 29 kDa), and GAPDH (1:10000; Rabbit; ab181602, Abcam, 36 kDa).

2.12 | Statistical analysis

Based on the statistical analysis that conducted by Graphpad prism 8.0, measurement data were expressed as mean ± standard deviation (SD). The comparison on expression difference in LIFR-AS1 in adjacent and SOC tissues was conducted by paired sample t test, and comparisons among multiple groups were performed using one-way analysis of variance (ANOVA) and followed by Bonferroni post hoc test. The enumeration data in Table 1 were compared by chi-square test. The statistical significance was indicated by p < 0.05.

3 | RESULTS

3.1 | Low expression of LIFR-AS1 in SOC was associated with the poor prognosis of SOC patients

As depicted in Figure 1A, TCGA-OV database indicated that LIFR-AS1 expression was remarkably lowered in tumor samples as compared to that in healthy samples, and Starbase revealed that the low expression of LIFR-AS1 was associated with poor survival of SOC (Figure 1A, p = 0.018). In addition, the result of qRT-PCR further confirmed that LIFR-AS1 expression was lower in SOC tissues than that in adjacent tissues (Figure 1B, p < 0.001). Moreover, compared with SOC tissues, the adjacent tissues were obviously stained brown (Figure 1C), demonstrating that LIFR-AS1 expression was largely
decreased in SOC tissues. Besides, low expression of LIFR-AS1 in SOC was associated with higher levels of tumor size, clinical stage, lymph node metastasis, and distant metastasis ($p < 0.05$, Table 1).

3.2 | LIFR-AS1 overexpression inhibited viability and proliferation of SOC cells while silencing LIFR-AS1 had the opposite effect

Subsequently, we detected the LIFR-AS1 expression in normal (HOSE) and SOC cells (A2780, OV-56, SK-OV-3, OVCAR3). In SOC cell lines, LIFR-AS1 expression was lower in SOC cells than that in HOSE cells, and among these SOC cells, LIFR-AS1 in OV-56 cells exhibited the highest expression ($p < 0.01$) and SK-OV-3 cells presented the lowest expression ($p < 0.001$, Figure 2A). Because SK-OV-3 and A2780 cells showed the most significant difference, we selected these two kinds of cells in the following experiments. Thereafter, the transfection of LIFR-AS1 overexpression plasmid or sh-LIFR-AS1 into A2780 and SK-OV-3 cells was successfully conducted that overexpression or silencing vector observably up-regulated or down-regulated the expression of LIFR-AS1 ($p < 0.05$, Figure 2B). It is worth noting that LIFR-AS1 overexpression contributed to the decrease in cell viability and proliferation, while LIFR-AS1 knockdown exerted the opposite effects ($p < 0.05$, Figure 2C–E).

3.3 | LIFR-AS1 overexpression inhibited the migration and invasion of SOC cells while silencing LIFR-AS1 had the opposite effect

As the data suggested, the migration rates of A2780 and SK-OV-3 cells were reduced by overexpressed LIFR-AS1 and elevated by sh-LIFR-AS1 ($p < 0.001$, Figure 3A,B). Additionally, LIFR-AS1 overexpression weakened the invasive ability of A2780 and SK-OV-3 cells ($p < 0.01$, Figure 3C,D), but LIFR-AS1 silencing exerted the opposite effect and enhanced the ability of cell invasion ($p < 0.001$, Figure 3C,D).

3.4 | LIFR-AS1 regulated the expressions of PCNA, cleaved caspase-3, E-cadherin, N-cadherin, and Snail in SOC cells

It can be observed in Figure 4 that LIFR-AS1 overexpression decreased the mRNA expressions of PCNA, N-cadherin, and Snail in
A2780 and SK-OV-3 cells (*p < 0.01, Figure 4A and D), while increasing E-cadherin expression (*p < 0.001, Figure 4A and D). Conversely, sh-LIFR-AS1 up-regulated the mRNA expressions of PCNA, N-cadherin, and Snail (*p < 0.01, Figure 4A and D), but down-regulated the expression of E-cadherin in A2780 and SK-OV-3 cells (*p < 0.05, Figure 4A and D). Simultaneously, the cleaved caspase-3 and E-cadherin protein expressions were increased (*p < 0.05, Figure 4B,C and 4E,F), while PCNA, N-cadherin, and Snail expressions were decreased in LIFR-AS1 group when compared to empty vector group (*p < 0.05, Figure 4B,C and 4E,F). Besides, LIFR-AS1 knockdown reversely regulated the protein expressions in A2780 and SK-OV-3 cells, which brought about the elevation of PCNA, N-cadherin, and Snail expressions (*p < 0.05, Figure 4B,C and 4E,F), and the reduction in cleaved caspase-3 and E-cadherin expressions (*p < 0.05, Figure 4B,C and 4E,F).

4 | DISCUSSION

As an important regulator, IncRNA has become a hotspot in researching SOC. Although IncRNAs could not encode protein, they can exert some effects on cellular behaviors such as cell proliferation, apoptosis, senescence, and migration by regulating the expressions of relevant functional genes.\(^{15}\) The study of Ni et al. showed that down-regulated LINC00515 is correlated with the tumor growth of SOC.\(^{28}\) Guo et al. proved that IncRNA SOCAR aggravates the development of SOC via the Wnt/β-catenin pathway.\(^{29}\) Additionally, Gokulnath et al. indicated that IncRNA HAND2-AS1 has the function to suppress the tumor growth of SOC.\(^{30}\) LIFR-AS1, which is an antisense IncRNA for the LIFR coding gene, has been noted that its aberrant expression is closely related to the pathogenesis and prognosis of patients with some tumors. The study by Okamura et al. found that LIFR-AS1 can...
inhibit the proliferation and migration of hepatocellular carcinoma (HCC) cells and is an important indicator of poor prognosis in HCC.\textsuperscript{31} Another study revealed that LIFR-AS1 up-regulation is positively correlated with more advanced and aggressive gastric cancer features.\textsuperscript{32}

Based on previous studies, this study explored the expression of LIFR-AS1 in SOC cells and its role in SOC progression. The results of this study signified that LIFR-AS1 was lowly expressed in SOC tissues and cells (A2780, OV-56, SK-OV-3, and OVCAR3). LIFR-AS1 overexpression could inhibit the cell viability, proliferation, migration, and invasion in A2780 and SK-OV-3 cells.

The indefinite proliferation and hampered apoptosis of the cells are the main characteristics of the tumor cells, such as SOC cells.\textsuperscript{33,34} PCNA is a nuclear protein widely expressed in S phase of cell cycle and is only synthesized and expressed in proliferative cells. The positive expression of PCNA indicates that the cell is in proliferative state.\textsuperscript{35,36} As a tumor marker protein, PCNA can reflect the synthesis and metabolism of RNA and DNA in tumor cells. Its expression level can be measured to assess the proliferative activity of tissues and various cancer cells, contributing to better determining progression, aggressiveness, and prognosis of the lesions.\textsuperscript{36} It has proved that down-regulation of the expression of PCNA repressed G1/S cell cycle transition of human OC cells.\textsuperscript{37} Additionally, IncRNA DLX6-AS1 inhibited the proliferation of OC cells via reducing the expression of PCNA.\textsuperscript{38} Caspase-3 is the most important final executor of apoptosis in caspase family and has a strong ability to induce apoptosis.\textsuperscript{39} Studies evidenced that IncRNA NNT-AS1 knockdown or IncRNA PCAT-1 overexpression weakens the activity of caspase-3 to impede the apoptosis of human OC cells.\textsuperscript{40,41} Similar to these studies, our

**FIGURE 4**  Effects of LIFR-AS1 on the expressions of genes related to proliferation and epithelial-mesenchymal transition in SOC cells. (A) The mRNA expressions of PCNA, E-cadherin, N-cadherin, and Snail in A2780 cells were measured by qRT-PCR. GAPDH was served as the internal reference. (B,C) The protein expressions of PCNA, cleaved caspase-3, E-cadherin, N-cadherin, and Snail in A2780 cells were detected by Western blot. GAPDH was employed as the internal reference. (D) The mRNA expressions of genes related to proliferation and epithelial-mesenchymal transition in SK-OV-3 cells were measured by qRT-PCR. GAPDH was served as the internal reference. (E,F) The protein expressions of genes related to proliferation and epithelial-mesenchymal transition in SK-OV-3 cells were determined by Western blot. GAPDH was served as the internal reference. All experiments were repeated three times to average. The data from three independent experiments were presented as the mean ± SD: *\(p < 0.05\); **\(p < 0.01\); ***\(p < 0.001\) vs. Empty vector. Abbreviation: qRT-PCR, quantitative real-time PCR; GAPDH, glyceraldehyde-3-phosphate dehydrogenase; PCNA, proliferating cell nuclear antigen; SD, standard deviation.
study got the knowledge that LIFR-AS1 overexpression decreased the expression of PCNA and increased the cleaved caspase-3 expression of SOC cells, and silencing of LIFR-AS1 reversely regulated these expressions, indicating that LIFR-AS1 overexpression hindered proliferation and induced apoptosis of SOC cells by regulating the levels of related molecules.

Invasion and metastasis are important contributors to the vast majority of tumor-associated metastasis and recurrence. Epithelial-mesenchymal transition (EMT) is an important mechanism of invasion and metastasis. It refers to the pathophysiological process of epithelial cells with polar and tight adhesion into non-polar and highly mobile stromal cells. EMT has been observed in a variety of human malignant tumors, including SOC. In this study, we detected the expressions of three EMT-related proteins, including E-cadherin, N-cadherin, and Snail. E-cadherin participates in the adhesion and connection between homotypic cells and maintains cell polarity, which plays an important role in maintaining the integrity of epithelial cell morphology and tissue structure. The overexpression of E-cadherin protein may inhibit tumor occurrence and metastasis, while the effect of N-cadherin is opposite to that of E-cadherin, and its expression can promote tumor invasion and metastasis. Besides, Snail, as one of EMT-related transcription factors, could regulate the expression level of E-cadherin, and is also a key factor in EMT. Massive amounts of evidence proved that IncRNAs enhance the migratory and invasive abilities of OC or SOC cells via regulating the EMT-regulated genes. For instance, IncRNA OIP5-AS1 up-regulates Snail expression to promote OC cell invasion and migration. IncRNA EBIC promotes metastasis of OC cells through up-regulating the E-cadherin expression, and IncRNA HAL suppresses the metastasis of SOC cells by regulating the expressions of E-cadherin and N-cadherin to inhibit EMT signaling pathway. Consistent with the results described in the previous literature, our study discovered that LIFR-AS1 overexpression facilitated an anti-metastatic phenotype in SOC by regulating EMT-related genes. Concretely, LIFR-AS1 overexpression increased the expression of E-cadherin, but decreased N-cadherin and Snail expressions. Moreover, silencing LIFR-AS1 regulated these expressions in a reverse way.

To sum up, our study demonstrates that LIFR-AS1 expression is down-regulated in SOC, and LIFR-AS1 overexpression inhibits SOC cell viability, proliferation, invasion, and migration by regulating the expressions of PCNA, cleaved caspase-3, and EMT-related genes. Our findings may provide the potential of LIFR-AS1, as a therapeutic target for SOC.

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Not applicable.

CONFLICT OF INTEREST
The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT
The analyzed data sets generated during the study are available from the corresponding author on reasonable request.

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