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Original Article

LncRNA CDIPTOSP-induced destabilization of KLF17 promotes ovarian cancer progression through STAU1-mediated mRNA decay

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Abstract: Ovarian cancer (OC) remains one of the most lethal gynecologic malignancies, largely due to its poorly understood pathogenesis, which limits the development of effective early detection and targeted therapy. This study was designed to explore the potential role of the long non-coding RNA CDIPTOSP in OC progression. We observed high expression of CDIPTOSP in OC tissues and cell lines. Knockdown of CDIPTOSP impeded the proliferation and migration of OC cells. Using the RNA pull-down-Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) approach, we found that CDIPTOSP bound staufen double-stranded RNA binding protein 1 (STAU1). In turn, CDIPTOSP-STAU1 interactions were essential for KLF transcription factor 17 (KLF17) mRNA destabilization. Notably, depletion of KLF17 could rescue the tumor-suppressive effects caused by CDIPTOSP knockdown, whereas overexpression of KLF17 abolished the tumor-promoting effects induced by overexpressing CDIPTOSP. In conclusion, our study provided the first evidence of the CDIPTOSP/STAU1/KLF17 axis in the regulation of OC progression.

Keywords: CDIPTOSP, ovarian cancer, STAU1, KLF17

Introduction

Ovarian cancer (OC) refers to epithelial cancer that occurs in the ovary or fallopian tubes, as well as histologically similar primary peritoneal cancer [1-3]. According to estimates, approximately 5% to 10% of women will be diagnosed with ovarian tumors at some stage in their lives [4]. Its incidence is 313,959 cases per year, with 207,252 deaths annually [5]. Epithelial ovarian cancer is the most common type of OC. Due to its insidious onset and poorly understood molecular mechanisms, early detection rates remain low, and the 5-year survival rate is only 45.6%. If the underlying mechanisms of OC initiation and progression could be elucidated, it would provide a critical foundation for improving early intervention, therapeutic strategies, and patient outcome [6-8]. Therefore, identifying the key molecular drivers of OC pathogenesis remains a significant challenge.

Using high-resolution microarrays and large-scale parallel sequencing technologies, it has been estimated that only 1.5% of the human genome encodes protein-coding genes, while over 98% of the human genome is transcribed into RNA transcripts without apparent protein-coding potential [9-12]. The long non-coding RNAs (lncRNAs) are defined as non-protein-coding transcripts longer than 200 nucleotides [13]. lncRNAs exert regulatory roles by interacting with proteins [14], DNA [15], or RNA [16, 17], participating in gene transcription, cell cycle regulation, and by epigenetic chromatin modifications [18, 19]. Recent studies have indicated that lncRNAs function as oncogenes or tumor suppressors and play crucial roles in tumori-

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genesis and metastasis. For instance, the long non-coding RNA NRSN2-AS1 not only stimulates proliferation and migration of OC cells by the PTK2/β-catenin pathway [20] but may also facilitate OC progression through the miR-744-5p/PRKX axis [21]. Another illustration is provided by the lncRNA GLCC1, which directly interacts with the HSP90 chaperone to stabilize the ubiquitination of the c-Myc transcription factor. This interaction specifies the transcriptional modification pattern of c-Myc target genes, thereby reshaping glycolytic metabolism to fuel colorectal cancer (CRC) proliferation [22]. Furthermore, LINC01554 is a novel tumor suppressor gene in hepatocellular carcinoma (HCC), facilitating ubiquitin-mediated degradation of PKM2, inhibiting the AKT/mTOR signaling pathway, abolishing aerobic glycolysis in HCC cells, and thus suppressing the progression of HCC [23]. In addition, the tissue-specific expression patterns of lncRNAs distinguish them from miRNAs and protein-coding mRNAs [10]. Due to their tissue specificity and widespread expression, they serve as precise biomarkers for cancer diagnosis, offering promising avenues for clinical applications [24-26].

CDIPTOSP, also known as CDIPT-AS1 or lncCTHCC, is a cancer-testis-associated long noncoding RNA (CT-lncRNA) located at chromosome region 16p11.2. Limited studies have indicated that CDIPTOSP is highly expressed in HCC, and it interacts with heterogeneous nuclear ribonucleoprotein K (hnRNP K) and promotes HCC progression by activating transcriptional coactivator YAP1, suggesting its potential as a prognostic marker and therapeutic target for HCC patients [27]. Nevertheless, the regulatory mechanisms of CDIPTOSP in other tumors still unknown.

In this study, we observed a significant upregulation of CDIPTOSP in human OC tissues compared to normal tissues. Silencing of CDIPTOSP in OC cells led to a marked inhibition of proliferation and migration. Using RNA pull-down coupled with liquid chromatography-tandem mass spectrometry (RNA pull-down-LC-MS/MS), we identified staufen double-stranded RNA binding protein 1 (STAU1) as the interactor with CDIPTOSP. Knockdown of STAU1 phenocopied the effects of CDIPTOSP loss. Additionally, RNA-Seq analysis revealed KLF transcription factor 17 (KLF17) as a common target of CDIPTOSP and STAU1. Importantly, CDIPTOSP bound to the 3'untranslated region (3'UTR) of KLF17 mRNA so that CDIPTOSP facilitated the degradation of KLF17 mRNA via STAU1-mediated mRNA decay (SMD). These findings provide novel mechanistic insight into the CDIPTOSP/STAU1/KLF17 signaling pathway, highlighting mechanistic biomarkers and therapeutic targets for OC intervention.

Materials and methods

Bioinformatic analysis

Clinical and gene expression information was obtained from The Cancer Genome Atlas (TCGA), Genotype-Tissue Expression (GTEx) project, and the Gene Expression Omnibus (GEO) database (GSE74448 and GSE119056). Survival analysis was performed using Kaplan-Meier (KM) survival curves, which allowed us to evaluate the survival probabilities of OC patients over time. Additionally, Receiver Operating Characteristic (ROC) curves were employed for diagnostic analysis.

Sample collection

OC and paracancerous tissues were derived from 18 adult patients who underwent surgery from March 2021 to January 2023 at the Suzhou Municipal Hospital. All patients received written informed consent and participant information was fully protected. The study was approved by the Research Ethics Committee of Suzhou Municipal Hospital, and written informed consent was obtained from all participants in accordance with the guidelines of the Declaration of Helsinki.

RNA extraction and RT-qPCR assay

Total RNA was extracted from tissue samples ground into powder and cells were transfected for 48 hours using TRIzol reagent (Vazyme, Nanjing, China). Subsequently, reverse transcription was performed using the HiScript III RT SuperMix for qPCR kit (Vazyme) in accordance with the manufacturer's instructions. Gene expression levels were quantified using the Taq Pro Universal SYBR qPCR Master Mix (Vazyme), along with a qRT-PCR system (Applied Biosystems, Foster City, CA, USA). Finally, the relative expression of genes was analyzed using the $2^{-\Delta\Delta CT}$ method and normalized to

18sRNA. The primers used were as outlined below: 18sRNA-F: 5'-AAACGGCTACCACATCCAAG-3', 18sRNA-R: 5'-CCTCCAATGGATCCTCGTTA-3'; CDIPTOSP-F: 5'-CCAAACGCGCATTCTTCACC-3', CDIPTOSP-R: 5'-GAGCATCTCCCTTGAAGCCT-3'; STAU1-F:5'-AATTGCTCCTCTCAGCCACC-3',STAU1-R: 5'-CACCTCCCACACACAGACAT-3'; KLF17-F: 5'-GCTGCTGGTCCTTAGGTGAA-3', KLF17-R: 5'-AGCCTTGTTGCGCTCAGTAT-3'.

Cell culture, si-RNA, plasmid, reagents, and transfection

OC cell lines (SKOV3, A2780, OVCAR3, HO8910 and CaoV3) and a normal ovarian epithelial cell line (IOSE80) were obtained from the Cell Bank of Chinese Academy of Sciences (Shanghai, China), and cultured in a humidified incubator at 37°C with 5% CO_2. RPMI-1640 medium (Gibco, USA) supplemented with 1% penicillin/streptomycin (PS) (NCM Biotech, China) and 10% fetal bovine serum (FSP500, ExCell Bio, China) was used to culture IOSE80, SKOV3, A2780, HO8910 and CaoV3 cells. OVCAR3 cells were cultured in RPMI-1640 medium containing 20% fetal bovine serum. SiRNAs (Gene Pharma, Shanghai, China) targeting CDIPTOSP, STAU1, and a negative control (si-NC) were transfected into SKOV3 and A2780 cells using Lipofectamine 2000 (Invitrogen, USA), as previously described [28, 29]. The siRNA target sequences were as follows: si-CDIPTOSP-1#: 5'-GCACUGCUUGCUGCCACUU-3'; si-CDIPTOSP-2#: 5'-CCUUCAAAGUGUUCUGGAU-3'; si-STAU1-1#: 5'-CCAUUUCCAGUUCCACCUU-3'; si-STAU1-2#: 5'-GCCUGCAGUUGAACGAGUA-3'; si-NC: 5'-UUCUCCGAACGUGUCACGU-3'.

All DNA plasmids used in this study were constructed and purchased from Genepharma. X-treme GENE HP DNA Transfection Reagent (Roche, Switzerland) was used for transfecting the plasmids into the cells according to the manufacturer's instructions. Cells were harvested 48 hours after transfection.

Cell proliferation assay

For the Cell Counting Kit 8 (CCK-8) assays, transfection with siRNAs or plasmids after 48 h, equal amounts of SKOV3 and A2780 cells were inoculated into 96-well plates (2000 cells/well). Next, we treated the cells with CCK-8 reagent (Beyotime, Shanghai, China) at 0, 24, 48, 72, and 96 hours. Subsequently, cell viability was assessed by measuring the optical density at 450 nm using a microplate reader as previously described [30, 31].

In the colony formation assay, cells were transfected for 48 hours and seeded in 6-well plates with equal amounts. After two weeks, the cells were fixed using methanol and stained with a 0.1% crystal violet solution.

Transwell assay

For the transwell assays, 48 hours post-transfection, 3.5×10^4 cells were seeded into the upper chamber of 24-well transwell (pore size 8 μm) and 300 μL of serum-free medium. Concurrently, 700 μL of complete medium was introduced into the lower chamber. After 36 hours of incubation, cells that had migrated from the upper chamber to the lower chamber were fixed in methanol, stained with crystal violet, and subsequently imaged and counted in three randomly selected fields under a microscope.

RNA pull-down assay

CDIPTOSP was transcribed *in vitro* using T7 RNA polymerase (Ambio Life, Shanghai, China). Next, the transcript was purified using the RNeasy Plus Mini kit (Qiagen) and treated with RNase-free DNase I (Qiagen). Following purification, the CDIPTOSP transcript was labeled with biotin using the Biotin RNA-Labeling Mix (Ambio Life). RNA pull-down experiments were subsequently performed using the Pierce Magnetic RNA-Protein Pull-Down Kit (Thermo Scientific). Finally, the interacting proteins with CDIPTOSP were determined through LC-MS/MS analysis, as previously described [32-34]. In brief, proteins in the clarified supernatant were fractionated using SDS-PAGE. Gel slices were excised and cut into small cubes (~1 mm^3) to allow for in-gel digestion with trypsin. After digestion, the recovered peptides were desalted on StageTips (Thermo Scientific) and subsequently analyzed by an LTQ Orbitrap Velos mass spectrometer (Thermo Scientific). For protein identification, MS/MS spectra were searched against the UniProt database, with a false discovery rate (FDR) threshold of 1% applied to both peptide and protein identifications. Protein abundances were determined using the label-free quantification (LFQ) algorithm integrated into MaxQuant.

RNA immunoprecipitation (RIP) assay

We used the Magna RIP™ RNA-Binding Protein Immunoprecipitation Kit (Millipore, USA) for the RIP assay following the manufacturer's instructions. OC cells were lysed in RIP lysis buffer, and 100 μL of the extracted proteins were incubated overnight at 4°C with anti-STAU1 (Proteintech) or IgG (Abcam) antibodies. Subsequently, the protein-RNA complexes were captured by the magnetic beads and the proteins were then eliminated using 0.5 mg/mL proteinase K. Ultimately, the purified RNAs were analyzed by RT-qPCR to determine the combination between STAU1 protein and CDIPTOSP.

RNA-Seq

RNA-Seq on SKOV3 cells was performed by LC-Bio Technology (Hangzhou, China), involving library preparation with poly-A enrichment, cDNA synthesis, and sequencing on an Novaseq™ 6000 platform. Quality control was performed with FastQC, and reads were processed with Trimmomatic before alignment to the human reference genome using STAR aligner. Transcript quantification was achieved with featureCounts, and differential expression analysis was carried out using DESeq2. Differentially expressed transcripts (DETs) were defined with fold change >2 and false discovery rate (FDR) <0.05.

RNA stability assay

OC cells transfected with siRNA or plasmid vectors were treated with 1 μg/mL actinomycin D (an inhibitor for gene transcription) for 0-9 hours. and collected at 3-hour intervals. The total cellular RNA was extracted and qRT-PCR was conducted to detect the relative mRNA levels.

Luciferase reporter assay

SKOV3 and A2780 cells were cultured in 12-well plates. When the fusion rate of cells reached 60-70%, they were co-transfected with pcDNA3.1-COIPTOSP or its negative control vector (pcDNA3.1-empty vector, EV), and pGL6-KLF17-WT or pGL6-KLF17-MUT luciferase reporter plasmids (Beyotime). After 48 hours of transfection, the cells were harvested, lysed, and the luciferase activity was measured using the Dual-Luciferase Reporter Gene Assay System (Beyotime). The results were normalized based on the Renilla luciferase luminescence intensity.

Statistical analysis

GraphPad Prism 8.0 software was used for statistical analysis. Unpaired Student's t-tests (for two groups) or one-way analysis of variance (ANOVA) (for multiple groups) were used for comparisons. Data are presented as mean ± standard deviation (SD). $P<0.05$ was considered significant.

Results

COIPTOSP expression is significantly upregulated in human OC tissues and cells

To investigate the association between CDIPTOSP and the occurrence and development of OC, we analyzed the expression level of CDIPTOSP using normal tissue and ovarian cancer samples from TCGA, GTEx, and GEO (GSE74448 and GSE119056) databases. We observed a significant increase in the expression of CDIPTOSP in tumor tissues compared to normal tissues (**Figure 1A-C**). Further analysis based on TCGA revealed that high levels of CDIPTOSP were associated with a poorer overall survival (OS) (**Figure 1D**). To validate these findings, we performed qRT-PCR on OC and adjacent non-cancerous tissues and our results confirmed that CDIPTOSP was indeed highly expressed in OC tissues (**Figure 1E**). Furthermore, the expression levels of CDIPTOSP in OC cell lines (SKOV3, A2780, HO8910, CaoV3) were also higher than in normal ovarian epithelial cells (IOSE80) (**Figure 1F**). In conclusion, the above findings suggested that CDIPTOSP may play a crucial role in regulating the progression of OC.

CDIPTOSP is required for OC cell proliferation and migration

To assess the role of CDIPTOSP in the advancement of OC in vitro, we conducted functional experiments on SKOV3 and A2780 cells that expressed high levels of CDIPTOSP (**Figure 1F**). Initially, we transfected SKOV3 and A2780 cells with two independent siRNAs (si-CDIPTOSP-1# and si-CDIPTOSP-2#) which both significantly decreased CDIPTOSP expression levels, as measured by qRT-PCR (**Figure 2A**, **2B**). CCK-8 and colony formation experiments showed that

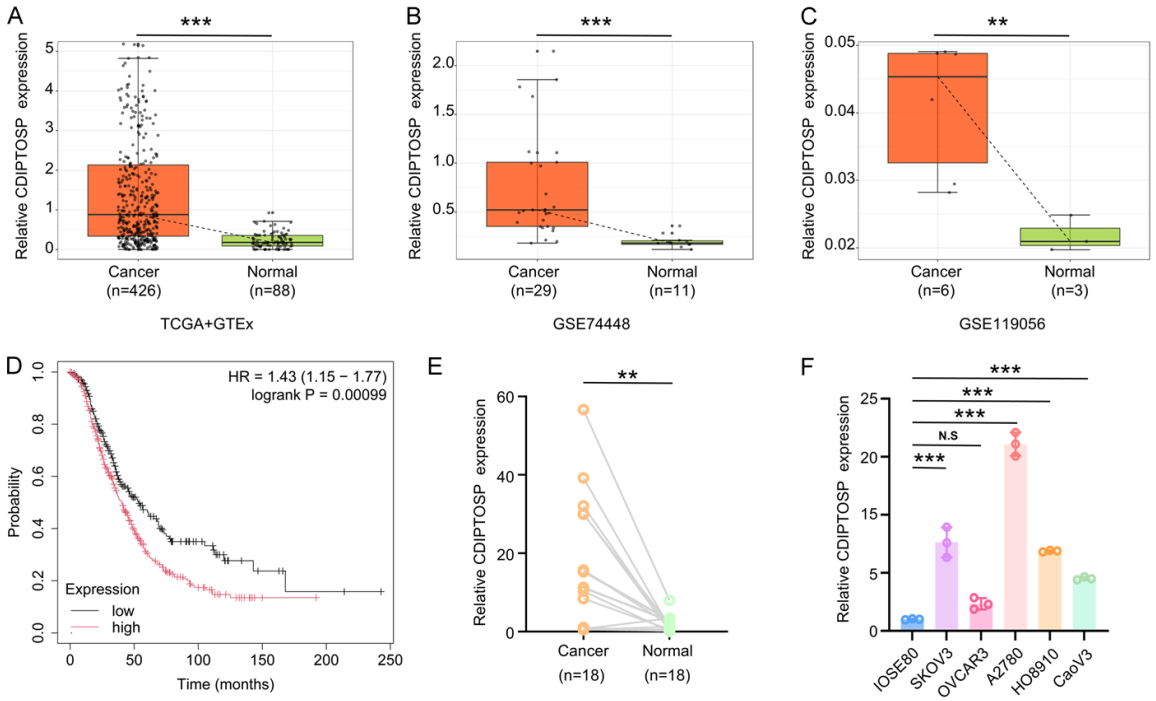

Figure 1. CDIPTOSP is overexpressed in both ovarian cancer (OC) tissues and cell lines. (A-C) Relative expression of CDIPTOSP in OC and normal tissues based on TCGA+GTEx (A), GSE74448 (B), and GSE119056 (C) datasets. (D) Kaplan-Meier curves for overall survival (OS) in OC patients. (E) Relative expression of CDIPTOSP in 18 paired OC samples. (F) Relative expression of CDIPTOSP in normal human ovarian epithelium cell (IOSE80) and OC cells (SKOV3, OVCAR3, A2780, HO8910 and CaoV3) (n=3). ***P*<0.01, ****P*<0.001, NS, not significant. Student's t test (A-C, E); one-way ANOVA with Dunnett's post hoc test (F).

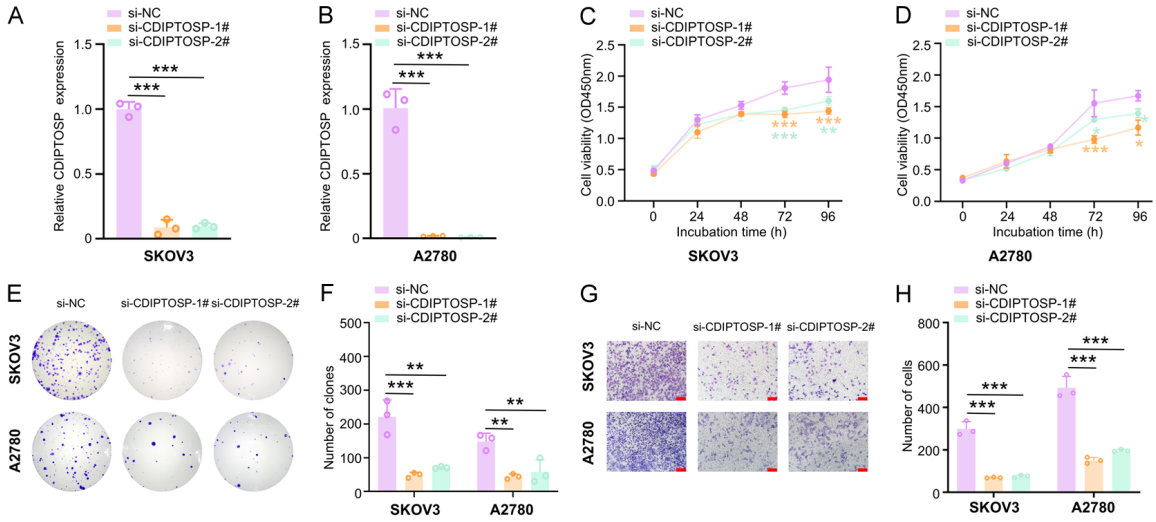

Figure 2. Silencing CDIPTOSP inhibits the proliferation and migration of ovarian cancer (OC) cells. (A, B) qRT-PCR analysis of CDIPTOSP expression in OC cells (SKOV3 and A2780) transfected with negative control siRNA (si-NC) or siRNAs targeting CDIPTOSP (si-CDIPTOSP-1# or si-CDIPTOSP-2#). n=3 per group. (C, D) The viability of OC cells transfected with si-CDIPTOSP or si-NC was assessed by Cell Counting Kit 8 (CCK-8) assay. n=6 per group. (E) Colony formation ability in OC cells transfected with si-CDIPTOSP or si-NC. n=3 per group. (F) Quantification of (E). (G) Transwell assays of OC cell migration transfected with si-CDIPTOSP or si-NC. n=3 per group. Scale bar: 100 μm. (H) Quantification of (G). **P*<0.05, ***P*<0.01, ****P*<0.001. One-way ANOVA with Dunnett's post hoc test.

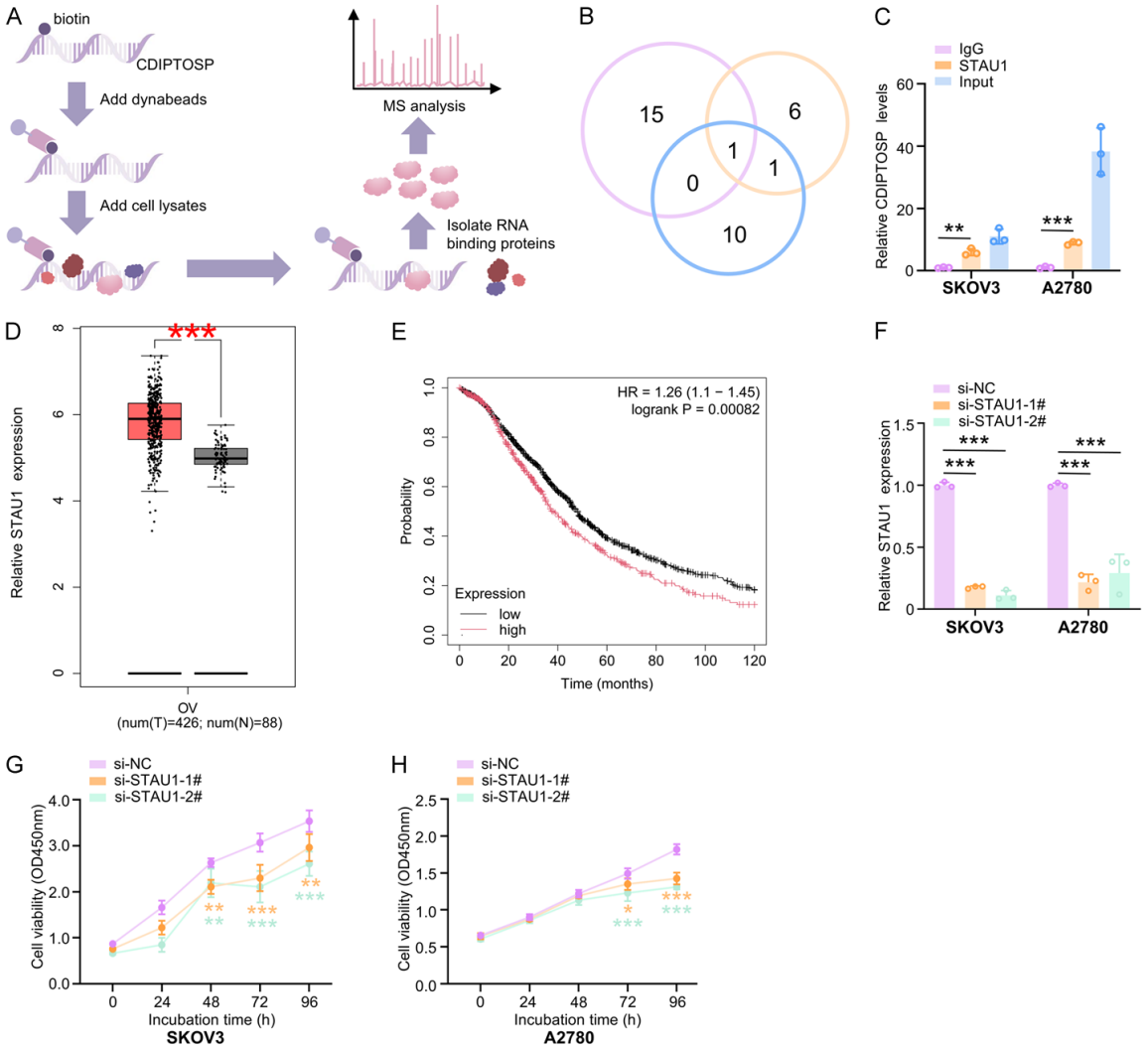

Figure 3. CDIPTOSP interacts with staufen double-stranded RNA binding protein 1 (STAU1), and STAU1 functions as an oncogene in OC cells. (A) Flow chart of the RNA pull-down-Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) assay. (B) Venn diagram showing the overlapping proteins identified by mass spectrometry in three independent RNA pull-down assays. (C) The levels of CDIPTOSP were quantified by RT-qPCR in STAU1-RIP assays performed on ovarian cancer (OC) cells (SKOV3 and A2780 cells). n=3 per group. (D) Relative expression of STAU1 in OC and normal tissues based on TCGA+GTEx datasets. (E) Kaplan-Meier curves for overall survival (OS) in OC patients. (F) STAU1 expression level in OC cells transfected with negative control siRNA (si-NC) or siRNAs targeting STAU1 (si-STAU1-1# or si-STAU1-2#). n=3 per group. (G, H) Cell viability was evaluated using Cell Counting Kit 8 (CCK-8) assays in OC cells transfected with si-NC or si-STAU1. n=6 per group. **P*<0.05, ***P*<0.01, ****P*<0.001. Student's t test (D); one-way ANOVA with Dunnett's post hoc test (C, F-H).

knockdown of CDIPTOSP inhibited proliferation of OC cells *in vitro* (**Figure 2C-F**). Transwell assays showed that the depletion of CDIPTOSP reduced the migration ability of OC cells (**Figure 2G**, **2H**).

CDIPTOSP interacts with STAU1, and STAU1 functions as an oncogene in OC

To further investigate the potential molecular mechanisms of CDIPTOSP in OC, we conducted RNA pull-down-LC-MS/MS analysis, unveiling potential protein candidates involved in the interaction with CDIPTOSP (**Figure 3A**). Venn diagram analysis of three independent experiments showed only one overlapping protein, STAU1 (**Figure 3B**). RIP-qPCR analysis confirmed the interaction between CDIPTOSP and STAU1 in OC cells (**Figure 3C**). Through TCGA and GTEx databases, we observed a significant increase in the expression of STAU1 in OC tissues compared to normal tissues (**Figure 3D**).

In addition, high levels of STAU1 were associated with a poorer overall survival (OS) (**Figure 3E**). Furthermore, two independent siRNAs (si-STAU1-1# or si-STAU1-2#) were transfected into OC cells to down-regulate CDIPTOSP expression (**Figure 3F**). CCK-8 assays demonstrated that downregulation of STAU1 reduced cell proliferation (**Figure 3G**, **3H**).

RNA-Seq reveals KLF17 as a downstream target of CDIPTOSP/STAU1

SMD is a STAU1-mediated mRNA degradation process, which STAU1 binds to the STAU1 binding site (SBS) as a complementary double-stranded RNA formed by base pairing of the Alu element between lncRNAs and the target mRNA 3'UTR, and then recruits RNA helicase and ATPase UPF1 to the target mRNA 3'UTR for mRNA degradation [35, 36]. To identify the downstream mRNA targeted by CDIPTOSP/STAU1 for degradation, we performed RNA-Seq analysis on SKOV3 cells transfected with si-NC, si-CDIPTOSP, and si-STAU1. Compared with si-NC group, we identified 773 upregulated transcripts and 706 downregulated transcripts in CDIPTOSP-knockdown group (**Figure 4A**, **4B**), and 939 upregulated transcripts and 780 downregulated transcripts in STAU1-knockdown group (**Figure 4C**, **4D**). Interestingly, there were 150 upregulated transcripts in the intersection of these two gene sets (**Figure 4E**). Among them, KLF transcription factor 17 (KLF17) has been identified as a tumor suppressor associated with many kinds of cancer, including colon cancer [37], gastric cancer [38], oral squamous cell carcinoma [39], lung adenocarcinoma [40], papillary thyroid carcinoma [41], hepatocellular carcinoma [42], and breast cancer [43]. Additionally, we predicted that CDIPTOSP and KLF17 3'UTR possess the ability to mutually bind, with their complementary sequences including Alu elements that can be targeted by STAU1 (**Figure 4F**, **4G**). Hence, we selected KLF17 for further study. In line with the RNA-Seq data, qPCR analysis confirmed a significant increase of KLF17 expression in si-CDIPTOSP and si-STAU1 OC cells compared to the si-NC group (**Figure 4H**, **4I**). Subsequently, we cloned both full-length and mutant (lacking Alu element) KLF17 3'UTR sequences into the pGL6 luciferase reporter vector. The luciferase reporter assay revealed that overexpression of CDIPTOSP significantly reduced luciferase activity in pGL6-KLF17 3'UTR-WT group compared to the control group, but had no obvious effect on the luciferase activity in pGL6-KLF17 3'UTR-MUT group (**Figure 4J**, **4K**). Furthermore, knockdown of CDIPTOSP and STAU1 significantly increased the stability of KLF17 mRNA (**Figure 4L**, **4M**). Taken together, we speculate that CDIPTOSP may bind to KLF17 3'UTR and promote KLF17 mRNA decay together with STAU1.

CDIPTOSP is required for STAU1-mediated KLF17 mRNA decay

Knockdown of CDIPTOSP significantly weakened the STAU1-KLF17 3'UTR interactions (**Figure 5A**, **5B**). RNA stability assay revealed that silencing CDIPTOSP markedly stabilized KLF17 mRNA which could not be reversed by overexpressing STAU1 (**Figure 5C**, **5D**). The above results indicated that CDIPTOSP is required for STAU1-mediated KLF17 mRNA decay by recruiting STAU1 to KLF17 3'UTR.

Moreover, we also observed that overexpression of CDIPTOSP significantly reduced KLF17 mRNA expression (**Figure 5E**, **5F**) and stability (**Figure 5G**, **5H**) in OC cells, which could be reversed by STAU1 knockdown (**Figure 5E-H**), indicating that CDIPTOSP regulates the stability of KLF17 mRNA in a STAU1-dependent manner.

KLF17 is involved in the oncogenic role of CDIPTOSP in OC

To investigate a potential association between KLF17 and CDIPTOSP in promoting OC progression, we carried out rescue experiments and found that simultaneous knockdown of CDIPTOSP and KLF17 significantly abolished the tumor-suppressive effects caused by CDIPTOSP knockdown alone (**Figure 6A**, **6B**). Similarly, overexpression of CDIPTOSP significantly increased the proliferation abilities of OC cells, which were subsequently reversed with simultaneous overexpression of CDIPTOSP and KLF17 (**Figure 6C**, **6D**). These findings demonstrated that CDIPTOSP promotes the proliferation of OC cells by targeting KLF17. In addition, receiver operating characteristic (ROC) curve analyses further suggested a potential prognostic value of the integrated CDIPTOSP/STAU1/KLF17 gene signature in OC (**Figure 7**).

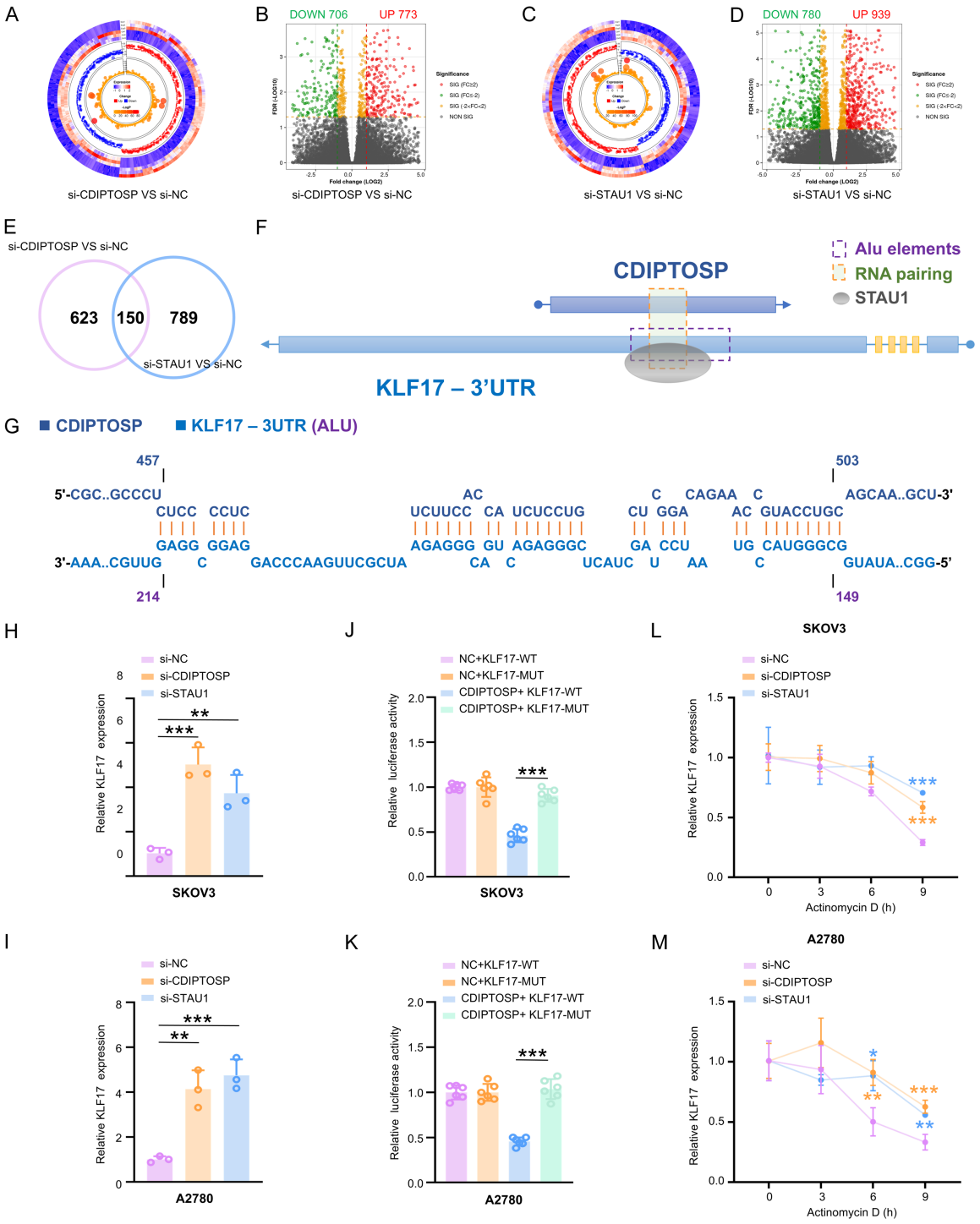

Figure 4. KLF17 is a major downstream target of CDIPTOSP and STAU1. (A, B) Circular heatmap (A) and volcano plot (B) showing the differentially expressed transcripts between the si-CDIPTOSP- and si-NC-transfected SKOV3 cells based on RNA-Seq. (C, D) Circular heatmap (C) and volcano plot (D) showing the differentially expressed transcripts between the si-STAU1- and si-NC-transfected SKOV3 cells based on RNA-Seq. For A to D, n=3 per group. (E) Venn diagram showing 150 overlapping transcripts that were up-regulated in the si-CDIPTOSP- and si-STAU1-treated cells. (F, G) Schematic diagram showing the predicted CDIPTOSP- KLF transcription factor 17 (KLF17) 3'UTR interactions based on base pairing. The binding sites contained Alu elements which can be recognized by STAU1. (H, I) qRT-PCR analysis of KLF17 expression in SKOV3 (H) and A2780 (I) cells transfected with si-NC, si-CDIPTOSP, or si-STAU1. n=3 per group. (J, K) Luciferase activity assays in SKOV3 (J) and A2780 (K) cells co-transfected with the indicated vectors. n=6 per group. (L, M) RNA stability assay showing the degradation rate of KLF17 mRNA in SKOV3 (L) and A2780 (M) cells transfected with si-CDIPTOSP and si-STAU1, and treated with actinomycin D for the indicated time-points. n=3 per group. $^{**}P<0.01$, $^{***}P<0.001$. One-way ANOVA with Dunnett's post hoc test.

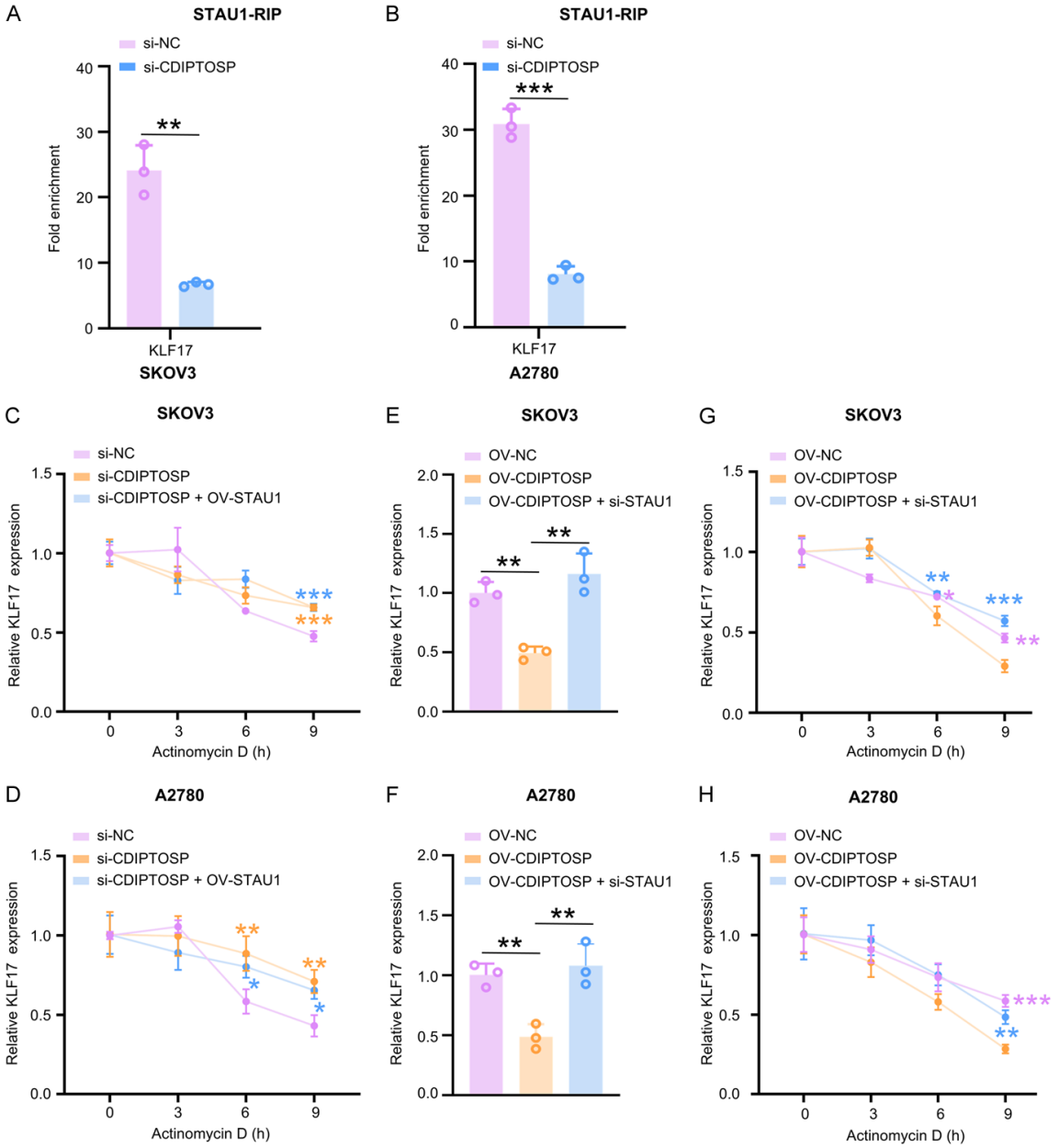

Figure 5. CDIPTOSP is required for STAU1-mediated KLF17 mRNA decay. (A, B) The levels of KLF17 transcripts were quantified by RT-qPCR in STAU1-RIP products performed on ovarian cancer (OC) cells transfected with si-NC and si-CDIPTOSP. n=3 per group. (C, D) RNA stability assay showing the degradation rate of KLF17 mRNA in SKOV3 (C) and A2780 (D) cells transfected with the indicated vectors and siRNAs, and treated with cycloheximide D for the indicated timepoints. n=3 per group. (E, F) qRT-PCR analysis of KLF17 expression in OC cells transfected with the indicated vectors and siRNAs. n=3 per group. (G, H) qRT-PCR analysis of the KLF17 expression following treating OC cells as indicated. si-NC combined with pcDNA3.1-empty vector (EV) was used as the control. n=3 per group. **P*<0.05, ***P*<0.01, ****P*<0.001. Student's t test (A, B); one-way ANOVA with Dunnett's post hoc test (C-H).

Discussion

Recent studies have shown that lncRNAs act as oncogenes or tumor suppressors in the occurrence and development of OC. For instance, lncRNA HOST2 is highly specifically expressed in epithelial OC. Inhibiting the expression of HOST2 significantly reduces the migration, invasion, and proliferation abilities of the OC cells [44]. Interestingly, lncRNA MEG3 expression was absent in more than 70% of OC tissues [45]. Overexpression of MEG3 can inhibit

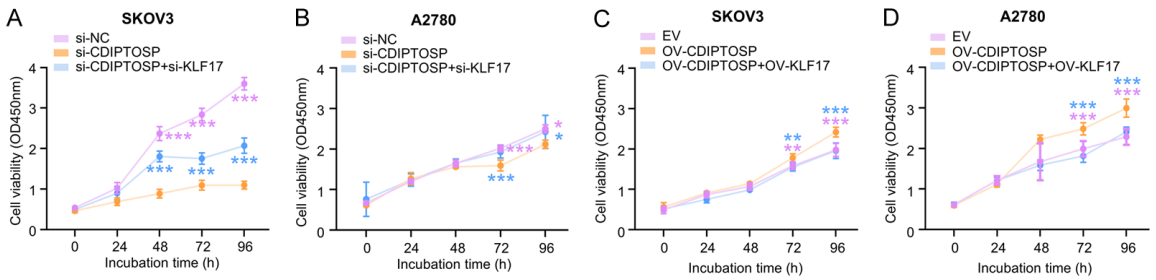

Figure 6. KLF17 is involved in CDIPTOSP-mediated tumor-promoting effects in ovarian cancer (OC) cells. A, B. CCK-8 assays of OC cells transfected with si-NC, si-CDIPTOSP, or si-CDIPTOSP+si-KLF17. n=6 per group. C, D. Cell Counting Kit 8 (CCK-8) assays of OC cells transfected with EV, pcDNA3.1-CDIPTOSP, or pcDNA3.1-CDIPTOSP+pcDNA3.1-KLF17. n=6 per group. **P*<0.05, ***P*<0.01, ****P*<0.001. One-way ANOVA with Dunnett's post hoc test.

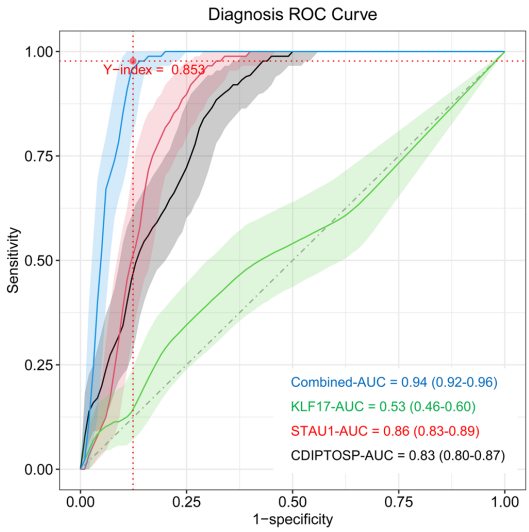

Figure 7. ROC curve analysis of CDIPTOSP, STAU1, KLF17, and integrated gene signature as potential diagnostic markers in ovarian cancer (OC).

the proliferation of OC cells and promote their apoptosis [46, 47]. In our study, we found that CDIPTOSP expression was significantly higher in OC tissues compared to normal tissues. Additionally, we determined the interaction between STAU1 and CDIPTOSP. CDIPTOSP binds to the 3'UTR of KLF17 mRNA and promotes the degradation of KLF17 mRNA through SMD, thereby facilitating the onset and progression of OC.

The double-stranded RNA-binding protein (dsRBP) Staufen, originally identified in Drosophila as a regulator of mRNA localization, has human homologs named Staufen1 (STAU1) and Staufen2 (STAU2) [48]. STAU1, a multifunctional dsRBP, is implicated in various cellular processes and cancer progression [49, 50]. It mediates mRNA localization [51], stability [52, 53], translation [54-56], and alternative splicing [57]. STAU1-mediated mRNA degradation (SMD) occurs through STAU1 binding to its site (SBS) within the 3' untranslated region (3'UTR) of target mRNA, recruiting the ATP-dependent RNA helicase UPF1 to promote mRNA degradation [35, 36]. Studies indicate that STAU1 exerts its SMD function with the involvement of lincRNA. For instance, the long non-coding RNA brain-derived neurotrophic factor antisense (BDNF-AS) induces the decay of retina and anterior neural fold homeobox 2 (RAX2) mRNA through SMD, impacting the malignant behavior of glioblastoma cells [58]. Similarly, lncRNA TINCR modulates the stability and expression of KLF2 mRNA by binding to STAU1, thereby influencing the transcription and expression of cyclin-dependent kinase genes CDKN1A/P21 and CDKN2B/P15, thus influencing the proliferation and apoptosis of gastric cancer cells [59]. Additionally, lncRNA HOXA11-AS interacts with STAU1, leading to the degradation of KLF2 mRNA, and promoting *in vivo* metastasis of gastric cancer [60]. However, there have been limited studies on lncRNA-dependent SMD in OC. Interestingly, our study revealed that CDIPTOSP interacts with STAU1 to enhance the proliferation of OC cells by SMD-mediated degradation of KLF17.

STAU1 binding sites include paired Alu elements and non-Alu sequences [55] within the mRNA 3'UTR. Alu elements, prevalent repetitive sequences in the human genome, serve as cis-regulatory elements influencing various aspects of protein-coding gene expression, including transcription initiation [61], alterna-

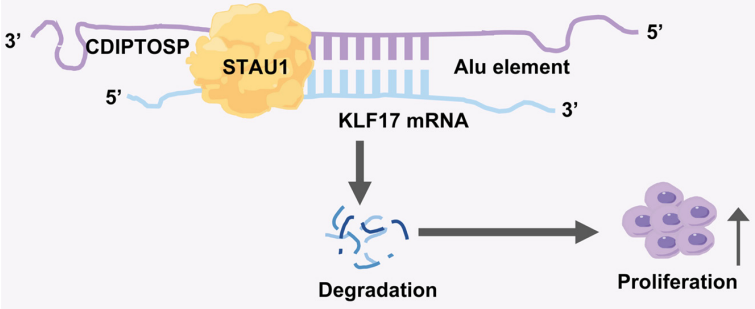

Figure 8. CDIPTOSP/STAU1/KLF17 axis model in OC progression. CDIPTOSP interacts with STAU1 and degrades KLF17 through STAU1-mediated SMD, thereby promoting ovarian cancer progression.

tive splicing [62], and translation initiation [63]. Studies have shown that lncRNA_AF087999 forms partially complementary double-stranded structures with Alu elements in the 3'UTR of plasminogen activator inhibitor type 1 (SERPINE1), and silencing STAU1 increases SERPINE1 mRNA levels [35]. In this study, we confirmed the interaction between CDIPTOSP and KLF17 3'UTR, and the paired sequence includes Alu elements. Luciferase activity assays demonstrated that mutating the Alu elements prevents CDIPTOSP from affecting the corresponding luciferase activity. Therefore, this implied that the SMD process mediated by CDIPTOSP/STAU1 was dependent on Alu elements.

Kruppel-like factor (KLF) is a subset of mammalian Sp/KLF zinc finger proteins [64, 65]. They play crucial roles in transcription by binding to specific DNA sequences, including G/C and CACCC boxes through highly conserved DNA binding domains (DBDs) or C-terminal regions [66, 67]. KLF is associated with tumor cell proliferation, invasion, and metastasis [68-70]. Among this family, KLF17 emerges as a tumor-suppressive transcription factor capable of impeding metastasis and Epithelial-Mesenchymal Transition (EMT) [71]. Studies indicate that KLF17 enhances TGF-β/Smad signaling through a Smad3-dependent pathway to inhibit human hepatocellular carcinoma growth and metastasis [72]. Overexpression of KLF17 can inhibit the growth of lung adenocarcinoma cells [73]. Up-regulating the expression of KLF17 may suppress epithelial-mesenchymal transition (EMT) through the TGF-β/Smad signaling pathway, leading to decreased invasion and migration of gastric cancer cells [38]. In our study, we discovered that knocking down KLF17 can counteract the growth inhibition of OC cells induced by CDIPTOSP knockdown. Conversely, overexpressing KLF17 mitigated the pro-cancer effects associated with CDIPTOSP overexpression. These findings suggested that KLF17 may also have functioned as a tumor suppressor in OC. However, this study does not provide a detailed explanation of how KLF17 inhibits the development and progression of OC, and further research is required.

Nevertheless, several limitations of this study should be acknowledged. First, although our *in vitro* experiments consistently support the oncogenic role of the CDIPTOSP/STAU1/KLF17 axis in ovarian cancer, the current findings lack *in vivo* validation using animal models. Such experiments, including subcutaneous or intraperitoneal tumorigenesis models with CDIPTOSP knockdown or overexpression, would provide more robust evidence for its functional significance in tumor growth and metastasis. Future studies incorporating *in vivo* approaches are warranted to strengthen the translational potential of our findings and to evaluate the therapeutic efficacy of targeting this axis in preclinical settings. Second, in the present study, the functional validation is primarily based on CCK-8 proliferation assays, and that future studies incorporating colony formation and apoptosis assays will be essential to confirm the long-term proliferative effects and to determine whether apoptosis contributes to the observed phenotypes.

Overall, our study described a novel mechanism of the CDIPTOSP/STAU1/KLF17 axis in OC progression (**Figure 8**). CDIPTOSP interacts with STAU1 and mediates the degradation of KLF17 mRNA by SMD, thereby enhancing the proliferation abilities of OC cells.

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Disclosure of conflict of interest

None.

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References

[1] Webb PM and Jordan SJ. Epidemiology of epithelial ovarian cancer. Best Pract Res Clin Obstet Gynaecol 2017; 41: 3-14.

[2] Meinhold-Heerlein I, Fotopoulou C, Harter P, Kurzeder C, Mustea A, Wimberger P, Hauptmann S and Sehouli J. The new WHO classification of ovarian, fallopian tube, and primary peritoneal cancer and its clinical implications. Arch Gynecol Obstet 2016; 293: 695-700.

[3] McCluggage WG. Morphological subtypes of ovarian carcinoma: a review with emphasis on new developments and pathogenesis. Pathology 2011; 43: 420-432.

[4] Lheureux S, Gourley C, Vergote I and Oza AM. Epithelial ovarian cancer. Lancet 2019; 393: 1240-1253.

[5] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A and Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021; 71: 209-249.

[6] Oronsky B, Ray CM, Spira AI, Trepel JB, Carter CA and Cottrill HM. A brief review of the management of platinum-resistant-platinum-refractory ovarian cancer. Med Oncol 2017; 34: 103.

[7] Roett MA and Evans P. Ovarian cancer: an overview. Am Fam Physician 2009; 80: 609-616.

[8] Chandra A, Pius C, Nabeel M, Nair M, Vishwanatha JK, Ahmad S and Basha R. Ovarian cancer: current status and strategies for improving therapeutic outcomes. Cancer Med 2019; 8: 7018-7031.

[9] Clark MB, Mercer TR, Bussotti G, Leonardi T, Haynes KR, Crawford J, Brunck ME, Cao KA, Thomas GP, Chen WY, Taft RJ, Nielsen LK, Enright AJ, Mattick JS and Dinger ME. Quantitative gene profiling of long noncoding RNAs with targeted RNA sequencing. Nat Methods 2015; 12: 339-342.

[10] Hauptman N and Glavač D. Long non-coding RNA in cancer. Int J Mol Sci 2013; 14: 4655-4669.

[11] Lander ES, Linton LM, Birren B, Nusbaum C, Zody MC, Baldwin J, Devon K, Dewar K, Doyle M, FitzHugh W, Funke R, Gage D, Harris K, Heaford A, Howland J, Kann L, Lehoczky J, LeVine R, McEwan P, McKernan K, Meldrim J, Mesirov JP, Miranda C, Morris W, Naylor J, Raymond C, Rosetti M, Santos R, Sheridan A, Sougnez C, Stange-Thomann Y, Stojanovic N, Subramanian A, Wyman D, Rogers J, Sulston J, Ainscough R, Beck S, Bentley D, Burton J, Clee C, Carter N, Coulson A, Deadman R, Deloukas P, Dunham A, Dunham I, Durbin R, French L, Grafham D, Gregory S, Hubbard T, Humphray S, Hunt A, Jones M, Lloyd C, McMurray A, Matthews L, Mercer S, Milne S, Mullikin JC, Mungall A, Plumb R, Ross M, Shownkeen R, Sims S, Waterston RH, Wilson RK, Hillier LW, McPherson JD, Marra MA, Mardis ER, Fulton LA, Chinwalla AT, Pepin KH, Gish WR, Chissoe SL, Wendl MC, Delehaunty KD, Miner TL, Delehaunty A, Kramer JB, Cook LL, Fulton RS, Johnson DL, Minx PJ, Clifton SW, Hawkins T, Branscomb E, Predki P, Richardson P, Wenning S, Slezak T, Doggett N, Cheng JF, Olsen A, Lucas S, Elkin C, Uberbacher E, Frazier M, Gibbs RA, Muzny DM, Scherer SE, Bouck JB, Sodergren EJ, Worley KC, Rives CM, Gorrell JH, Metzker ML, Naylor SL, Kucherlapati RS, Nelson DL, Weinstock GM, Sakaki Y, Fujiyama A, Hattori M, Yada T, Toyoda A, Itoh T, Kawagoe C, Watanabe H, Totoki Y, Taylor T, Weissenbach J, Heilig R, Saurin W, Artiguenave F, Brottier P, Bruls T, Pelletier E, Robert C, Wincker P, Smith DR, Doucette-Stamm L, Rubenfield M, Weinstock K, Lee HM, Dubois J, Rosenthal A, Platzer M, Nyakatura G, Taudien S, Rump A, Yang H, Yu J, Wang J, Huang G, Gu

J, Hood L, Rowen L, Madan A, Qin S, Davis RW, Federspiel NA, Abola AP, Proctor MJ, Myers RM, Schmutz J, Dickson M, Grimwood J, Cox DR, Olson MV, Kaul R, Raymond C, Shimizu N, Kawasaki K, Minoshima S, Evans GA, Athanasiou M, Schultz R, Roe BA, Chen F, Pan H, Ramser J, Lehrach H, Reinhardt R, McCombie WR, de la Bastide M, Dedhia N, Blöcker H, Hornischer K, Nordsiek G, Agarwala R, Aravind L, Bailey JA, Bateman A, Batzoglou S, Birney E, Bork P, Brown DG, Burge CB, Cerutti L, Chen HC, Church D, Clamp M, Copley RR, Doerks T, Eddy SR, Eichler EE, Furey TS, Galagan J, Gilbert JG, Harmon C, Hayashizaki Y, Haussler D, Hermjakob H, Hokamp K, Jang W, Johnson LS, Jones TA, Kasif S, Kaspryzk A, Kennedy S, Kent WJ, Kitts P, Koonin EV, Korf I, Kulp D, Lancet D, Lowe TM, McLysaght A, Mikkelsen T, Moran JV, Mulder N, Pollara VJ, Ponting CP, Schuler G, Schultz J, Slater G, Smit AF, Stupka E, Szustakowki J, Thierry-Mieg D, Thierry-Mieg J, Wagner L, Wallis J, Wheeler R, Williams A, Wolf YI, Wolfe KH, Yang SP, Yeh RF, Collins F, Guyer MS, Peterson J, Felsenfeld A, Wetterstrand KA, Patrinos A, Morgan MJ, de Jong P, Catanese JJ, Osoegawa K, Shizuya H, Choi S, Chen YJ and Szustakowki J; International Human Genome Sequencing Consortium. Initial sequencing and analysis of the human genome. Nature 2001; 409: 860-921.

[12] Stein LD. Human genome: end of the beginning. Nature 2004; 431: 915-916.

[13] Zhan L, Li J and Wei B. Long non-coding RNAs in ovarian cancer. J Exp Clin Cancer Res 2018; 37: 120.

[14] Wang C, Wang J, Shen X, Li M, Yue Y, Cheng X, Lu W, Wang X and Xie X. LncRNA SPOCD1-AS from ovarian cancer extracellular vesicles remodels mesothelial cells to promote peritoneal metastasis via interacting with G3BP1. J Exp Clin Cancer Res 2021; 40: 101.

[15] Yao RW, Wang Y and Chen LL. Cellular functions of long noncoding RNAs. Nat Cell Biol 2019; 21: 542-551.

[16] Jiang R, Zhang H, Zhou J, Wang J, Xu Y, Zhang H, Gu Y, Fu F, Shen Y, Zhang G, Feng L, Zhang X, Chen Y and Shen F. Inhibition of long noncoding RNA XIST upregulates microRNA-149-3p to repress ovarian cancer cell progression. Cell Death Dis 2021; 12: 145.

[17] Wang X, Li X, Lin F, Sun H, Lin Y, Wang Z and Wang X. The lnc-CTSLP8 upregulates CTSL1 as a competitive endogenous RNA and promotes ovarian cancer metastasis. J Exp Clin Cancer Res 2021; 40: 151.

[18] Li SY, Zhu Y, Li RN, Huang JH, You K, Yuan YF and Zhuang SM. LncRNA Lnc-APUE is repressed by HNF4α and promotes G1/S phase transition and tumor growth by regulating MiR-20b/E2F1 axis. Adv Sci (Weinh) 2021; 8: 2003094.

[19] Oncul S, Amero P, Rodriguez-Aguayo C, Calin GA, Sood AK and Lopez-Berestein G. Long noncoding RNAs in ovarian cancer: expression profile and functional spectrum. RNA Biol 2020; 17: 1523-1534.

[20] Wu YB, Li SY, Liu JY, Xue JJ, Xu JF, Chen T, Cao TY, Zhou H, Wu TT, Dong CL, Qian WF, Qiao LW, Hou SY, Wang T and Shen C. Long non-coding RNA NRSN2-AS1 promotes ovarian cancer progression through targeting PTK2/β-catenin pathway. Cell Death Dis 2023; 14: 696.

[21] Chen Q, Xie J and Yang Y. Long non-coding RNA NRSN2-AS1 facilitates tumorigenesis and progression of ovarian cancer via miR-744-5p/PRKX axis. Biol Reprod 2022; 106: 526-539.

[22] Tang J, Yan T, Bao Y, Shen C, Yu C, Zhu X, Tian X, Guo F, Liang Q, Liu Q, Zhong M, Chen J, Ge Z, Li X, Chen X, Cui Y, Chen Y, Zou W, Chen H, Hong J and Fang JY. LncRNA GLCC1 promotes colorectal carcinogenesis and glucose metabolism by stabilizing c-Myc. Nat Commun 2019; 10: 3499.

[23] Zheng YL, Li L, Jia YX, Zhang BZ, Li JC, Zhu YH, Li MQ, He JZ, Zeng TT, Ban XJ, Yuan YF, Li Y and Guan XY. LINC01554-mediated glucose metabolism reprogramming suppresses tumorigenicity in hepatocellular carcinoma via downregulating PKM2 expression and inhibiting Akt/mTOR signaling pathway. Theranostics 2019; 9: 796-810.

[24] Beg A, Parveen R, Fouad H, Yahia ME and Hassanein AS. Role of different non-coding RNAs as ovarian cancer biomarkers. J Ovarian Res 2022; 15: 72.

[25] Prensner JR, Iyer MK, Balbin OA, Dhanasekaran SM, Cao Q, Brenner JC, Laxman B, Asangani IA, Grasso CS, Kominsky HD, Cao X, Jing X, Wang X, Siddiqui J, Wei JT, Robinson D, Iyer HK, Palanisamy N, Maher CA and Chinnaiyan AM. Transcriptome sequencing across a prostate cancer cohort identifies PCAT-1, an unannotated lincRNA implicated in disease progression. Nat Biotechnol 2011; 29: 742-749.

[26] Shen C, Cao R, Zhou Q, Zhou T, Wu T, Gao W, Wang G, Feng G, Qiao L and Wang T. LINC00654 promotes ovarian cancer progression by facilitating nuclear export of HuR and stabilizing oncogenic mRNAs. Oncogene 2025; 44: 3422-3436.

[27] Xia A, Yuan W, Wang Q, Xu J, Gu Y, Zhang L, Chen C, Wang Z, Wu D, He Q, Yu W, Wang F, Xue C, Zhang Y, Bao G, Tao X, Liu S, Wang S, Hu Z and Sun B. The cancer-testis lncRNA lnc-CTHCC promotes hepatocellular carcinogenesis by binding hnRNP K and activating YAP1 transcription. Nat Cancer 2022; 3: 203-218.

[28] Lv J, Wu T, Xue J, Shen C, Gao W, Chen X, Guo Y, Liu M, Yu J, Huang X and Zheng B. ASB1 engages with ELOB to facilitate SQOR ubiquitination and H(2)S homeostasis during spermiogenesis. Redox Biol 2025; 79: 103484.
[29] Jiang B, Wang K, Hu H, Gao W, Shen C, Chen X, Huang X, Yu J, Wu Y and Zheng B. CRL2(LRRC41)-mediated DDX5 ubiquitination enhances interaction with ELAVL1 preventing NOG mRNA degradation and sustaining proliferation and migration of human spermatogonial stem cell-like cell line. BMC Biol 2025; 23: 247.
[30] Yu J, Shen C, Lin M, Chen X, Dai X, Li Z, Wu Y, Fu Y, Lv J, Huang X, Zheng B and Sun F. BMI1 promotes spermatogonial stem cell maintenance by epigenetically repressing Wnt10b/β-catenin signaling. Int J Biol Sci 2022; 18: 2807-2820.
[31] Hu H, Xi X, Jiang B, Wang K, Wu T, Chen X, Guo Y, Zhou T, Huang X, Yu J, Gao T, Wu Y and Zheng B. RNF187 facilitates proliferation and migration of human spermatogonial stem cells through WDR77 polyubiquitination. Cell Prolif 2025; 58: e70042.
[32] Zhou J, Li J, Qian C, Qiu F, Shen Q, Tong R, Yang Q, Xu J, Zheng B, Lv J and Hou J. LINC00624/TEX10/NF-κB axis promotes proliferation and migration of human prostate cancer cells. Biochem Biophys Res Commun 2022; 601: 1-8.
[33] Liu Y, Yu X, Huang A, Zhang X, Wang Y, Geng W, Xu R, Li S, He H, Zheng B, Chen G and Xu Y. INTS7-ABCD3 interaction stimulates the proliferation and osteoblastic differentiation of mouse bone marrow mesenchymal stem cells by suppressing oxidative stress. Front Physiol 2021; 12: 758607.
[34] Zhang K, Xu J, Ding Y, Shen C, Lin M, Dai X, Zhou H, Huang X, Xue B and Zheng B. BMI1 promotes spermatogonia proliferation through epigenetic repression of Ptprm. Biochem Biophys Res Commun 2021; 583: 169-177.
[35] Gong C and Maquat LE. lncRNAs transactivate STAU1-mediated mRNA decay by duplexing with 3'UTRs via Alu elements. Nature 2011; 470: 284-288.
[36] Kim YK, Furic L, Desgroseillers L and Maquat LE. Mammalian Staufen1 recruits Upf1 to specific mRNA 3'UTRs so as to elicit mRNA decay. Cell 2005; 120: 195-208.
[37] Yi S, Luo M, Peng Y, Chen Y and Yu D. Anti-oncogenic mechanism of KLF17 in colon cancer by repressing cell migration and invasion via FHL1 upregulation. Chin J Physiol 2023; 66: 534-545.
[38] Li S, Li Y, Tan B and An Z. Effect of KLF17 overexpression on epithelial-mesenchymal transition of gastric cancer cells. J Int Med Res 2021; 49: 3000605211051581.
[39] Lee YJ, Chan L, Yeh CM, Lee CH and Sung WW. Overexpression of KLF17 predicts a favorable prognosis in patients with oral squamous cell carcinoma: a retrospective study. Medicina (Kaunas) 2020; 56: 57.
[40] Cai XD, Che L, Lin JX, Huang S, Li J, Liu XY, Pan XF, Wang QQ, Chen L, Lin MJ, Huang ZH, Ma HM, Wu Y, Liu SM and Zhou YB. Krüppel-like factor 17 inhibits urokinase plasminogen activator gene expression to suppress cell invasion through the Src/p38/ MAPK signaling pathway in human lung adenocarcionma. Oncotarget 2017; 8: 38743-38754.
[41] Ye WC, Gao L, Huang J, Fang XM and Xie G. Suppressed Krüppel-like factor 17 expression induces tumor proliferation, metastasis and a poor prognosis in papillary thyroid carcinoma. Mol Med Rep 2014; 10: 2087-2092.
[42] Liu FY, Deng YL, Li Y, Zeng D, Zhou ZZ, Tian DA and Liu M. Down-regulated KLF17 expression is associated with tumor invasion and poor prognosis in hepatocellular carcinoma. Med Oncol 2013; 30: 425.
[43] Gumireddy K, Li A, Gimotty PA, Klein-Szanto AJ, Showe LC, Katsaros D, Coukos G, Zhang L and Huang Q. KLF17 is a negative regulator of epithelial-mesenchymal transition and metastasis in breast cancer. Nat Cell Biol 2009; 11: 1297-1304.
[44] Rangel LB, Sherman-Baust CA, Wernyj RP, Schwartz DR, Cho KR and Morin PJ. Characterization of novel human ovarian cancer-specific transcripts (HOSTs) identified by serial analysis of gene expression. Oncogene 2003; 22: 7225-7232.
[45] Al-Rugeebah A, Alanazi M and Parine NR. MEG3: an oncogenic long non-coding rna in different cancers. Pathol Oncol Res 2019; 25: 859-874.
[46] Braconi C, Kogure T, Valeri N, Huang N, Nuovo G, Costinean S, Negrini M, Miotto E, Croce CM and Patel T. microRNA-29 can regulate expression of the long non-coding RNA gene MEG3 in hepatocellular cancer. Oncogene 2011; 30: 4750-4756.
[47] Zhou Y, Zhong Y, Wang Y, Zhang X, Batista DL, Gejman R, Ansell PJ, Zhao J, Weng C and Klibanski A. Activation of p53 by MEG3 noncoding RNA. J Biol Chem 2007; 282: 24731-24742.
[48] St Johnston D, Beuchle D and Nüsslein-Volhard C. Staufen, a gene required to localize maternal RNAs in the Drosophila egg. Cell 1991; 66: 51-63.
[49] Almasi S and Jasmin BJ. The multifunctional RNA-binding protein Staufen1: an emerging regulator of oncogenesis through its various roles in key cellular events. Cell Mol Life Sci 2021; 78: 7145-7160.

[50] Tosar LJ, Thomas MG, Baez MV, Ibanez I, Chernomoretz A and Boccaccio GL. Staufen: from embryo polarity to cellular stress and neurodegeneration. Front Biosci (Schol Ed) 2012; 4: 432-452.
[51] Kanai Y, Dohmae N and Hirokawa N. Kinesin transports RNA: isolation and characterization of an RNA-transporting granule. Neuron 2004; 43: 513-525.
[52] Gong C, Kim YK, Woeller CF, Tang Y and Maquat LE. SMD and NMD are competitive pathways that contribute to myogenesis: effects on PAX3 and myogenin mRNAs. Genes Dev 2009; 23: 54-66.
[53] Kim YK, Furic L, Parisien M, Major F, DesGroseillers L and Maquat LE. Staufen1 regulates diverse classes of mammalian transcripts. EMBO J 2007; 26: 2670-2681.
[54] Sugimoto Y, Vigilante A, Darbo E, Zirra A, Militti C, D'Ambrogio A, Luscombe NM and Ule J. hiCLIP reveals the in vivo atlas of mRNA secondary structures recognized by Staufen 1. Nature 2015; 519: 491-494.
[55] Ricci EP, Kucukural A, Cenik C, Mercier BC, Singh G, Heyer EE, Ashar-Patel A, Peng L and Moore MJ. Staufen1 senses overall transcript secondary structure to regulate translation. Nat Struct Mol Biol 2014; 21: 26-35.
[56] Crawford Parks TE, Marcellus KA, Langill J, Ravel-Chapuis A, Michaud J, Cowan KN, Côté J and Jasmin BJ. Novel roles for Staufen1 in embryonal and alveolar rhabdomyosarcoma via c-myc-dependent and -independent events. Sci Rep 2017; 7: 42342.
[57] Bondy-Chorney E, Crawford Parks TE, Ravel-Chapuis A, Klinck R, Rocheleau L, Pelchat M, Chabot B, Jasmin BJ and Côté J. Staufen1 regulates multiple alternative splicing events either positively or negatively in DM1 indicating its role as a disease modifier. PLoS Genet 2016; 12: e1005827.
[58] Su R, Ma J, Zheng J, Liu X, Liu Y, Ruan X, Shen S, Yang C, Wang D, Cai H, Li Z and Xue Y. PABPC1-induced stabilization of BDNF-AS inhibits malignant progression of glioblastoma cells through STAU1-mediated decay. Cell Death Dis 2020; 11: 81.
[59] Xu TP, Liu XX, Xia R, Yin L, Kong R, Chen WM, Huang MD and Shu YQ. SP1-induced upregulation of the long noncoding RNA TINCR regulates cell proliferation and apoptosis by affecting KLF2 mRNA stability in gastric cancer. Oncogene 2015; 34: 5648-5661.
[60] Liu Z, Chen Z, Fan R, Jiang B, Chen X, Chen Q, Nie F, Lu K and Sun M. Over-expressed long noncoding RNA HOXA11-AS promotes cell cycle progression and metastasis in gastric cancer. Mol Cancer 2017; 16: 82.
[61] Cordaux R and Batzer MA. The impact of retrotransposons on human genome evolution. Nat Rev Genet 2009; 10: 691-703.
[62] Walters RD, Kugel JF and Goodrich JA. InvAluable junk: the cellular impact and function of Alu and B2 RNAs. IUBMB Life 2009; 61: 831-837.
[63] Häsler J and Strub K. Alu elements as regulators of gene expression. Nucleic Acids Res 2006; 34: 5491-5497.
[64] Ghaleb AM, Nandan MO, Chanchevalap S, Dalton WB, Hisamuddin IM and Yang VW. Krüppel-like factors 4 and 5: the yin and yang regulators of cellular proliferation. Cell Res 2005; 15: 92-96.
[65] Schuh R, Aicher W, Gaul U, Côté S, Preiss A, Maier D, Seifert E, Nauber U, Schröder C, Kemler R, et al. A conserved family of nuclear proteins containing structural elements of the finger protein encoded by Krüppel, a Drosophila segmentation gene. Cell 1986; 47: 1025-1032.
[66] Lomberk G and Urrutia R. The family feud: turning off Sp1 by Sp1-like KLF proteins. Biochem J 2005; 392: 1-11.
[67] van Vliet J, Crofts LA, Quinlan KG, Czolij R, Perkins AC and Crossley M. Human KLF17 is a new member of the Sp/KLF family of transcription factors. Genomics 2006; 87: 474-482.
[68] Suske G, Bruford E and Philipsen S. Mammalian SP/KLF transcription factors: bring in the family. Genomics 2005; 85: 551-556.
[69] Black AR, Black JD and Azizkhan-Clifford J. Sp1 and krüppel-like factor family of transcription factors in cell growth regulation and cancer. J Cell Physiol 2001; 188: 143-160.
[70] Moore DL, Blackmore MG, Hu Y, Kaestner KH, Bixby JL, Lemmon VP and Goldberg JL. KLF family members regulate intrinsic axon regeneration ability. Science 2009; 326: 298-301.
[71] Ali A, Shah AS and Ahmad A. Gain-of-function of mutant p53: mutant p53 enhances cancer progression by inhibiting KLF17 expression in invasive breast carcinoma cells. Cancer Lett 2014; 354: 87-96.
[72] Ali A, Zhang P, Liangfang Y, Wenshe S, Wang H, Lin X, Dai Y, Feng XH, Moses R, Wang D, Li X and Xiao J. KLF17 empowers TGF-β/Smad signaling by targeting Smad3-dependent pathway to suppress tumor growth and metastasis during cancer progression. Cell Death Dis 2015; 6: e1681.
[73] Cai XD, Zhou YB, Huang LX, Zeng QL, Zhang LJ, Wang QQ, Li SL, Feng JQ and Han AJ. Reduced expression of Krüppel-like factor 17 is related to tumor growth and poor prognosis in lung adenocarcinoma. Biochem Biophys Res Commun 2012; 418: 67-73.