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KCNMA1-AS1 attenuates apoptosis of epithelial ovarian cancer cells and serves as a risk factor for poor prognosis of epithelial ovarian cancer

S.-Y. MA[1], P. WEI[2], F. QU[3]

[1]Clinical Experimental Teaching Center/Department of Obstetrics and Gynecology, The First Affiliated Hospital/School of General Medicine of Xi'an Medical Universi-ty Xi'an, China
[2]Department of Gynecological Oncology, The Tumor Hospital of Shandong Province, Jinan, China
[3]Cancer Institute, the Fourth Hospital of Hebei Medical University, Shijiazhuang, China

Shuyun Ma and Ping Wei contributed equally to this work

Abstract. – OBJECTIVE: To explore the role of KCNMA1-AS1 in epithelial ovarian cancer (EOC) and its underlying mechanism.

PATIENTS AND METHODS: We first screened out the differentially expressed lncRNAs (KCNMA1-AS1) in the GEO (gene expression omnibus) database. The relationship between KCNMA1-AS1 expression and prognosis of EOC with different pathological types was analyzed by meta-analysis. Subsequently, KCNMA1-AS1 expressions in EOC tissues and normal ovarian tissues were detected by quantitative Real Time-Polymerase Chain Reaction (qRT-PCR). The correlation between KCNMA1-AS1 level with progression-free survival (PFS) and overall survival (OS) of EOC was analyzed. Furthermore, proliferation and migration of EOC cells transfected with the corresponding plasmids were analyzed by Cell Counting Kit-8 (CCK-8) and transwell assay, respectively. Apoptosis-related genes in EOC cells were detected by Western blot.

RESULTS: KCNMA1-AS1 was a risk factor for prognosis in high-grade, advanced and serous EOC. Upregulated KCNMA1-AS1 was found in EOC tissues than that of normal tissues, showing the diagnostic potential of KCNMA1-AS1 in EOC. Statistical analysis indicated that KCNMA1-AS1 was not correlated with the DFS, OS, age, histological type, lymph node metastasis and recurrence, but related to FIGO stage of EOC patients. For in vitro experiments, the proliferation and migration of were enhanced, and apoptosis of HO8910 cells overexpressing KCNMA1-AS1 was inhibited. Furthermore, elevated expressions of Caspase-3 and Caspase-9, as well as reduced expression of Bcl-xL, were observed after KCNMA1-AS1 knockdown in EOC cells.

CONCLUSIONS: KCNMA1-AS1 is overexpressed in EOC and negatively correlated with its prognosis. KCNMA1-AS1 participates in the occurrence and development of EOC by promoting proliferation, migration and inhibiting apoptosis of ovarian cancer cells via apoptosis pathway.

Key Words:
GEO database, Epithelial ovarian cancer, KCNMA1-AS1, Apoptosis.

Introduction

Epithelial ovarian cancer (EOC) is one of the most common gynecological malignancies. Globally, the incidence rate of EOC ranks the third of gynecological malignancies, and its mortality rate ranks the first[1,2]. Although the combination of ovarian cytoreductive surgery and first-line TP (taxol and platinum) chemotherapy can significantly relieve the symptoms, most of EOC patients experience tumor recurrence within 3 years. More seriously, the 5-year survival rate of EOC is only about 40%, and no remarkable improvement on overall survival of EOC has been made in the past 30 years[3,4]. Therefore, it is of great importance to investigate the pathogenesis of EOC.

Long non-coding RNAs (lncRNAs) are a class of RNAs with over 200 bp in length, which could not encode proteins[5]. LncRNAs were previously considered as transcription noises. In recent years, lncRNAs are believed to regulate cell differentiation, proliferation, apoptosis and other biological processes, especially in tumor cells[6,7]. Studies[8] have shown that UCA1 can upregulate MMP-14 by competitively binding to miRNA-485-5p, thus leading to stimulated invasive ability of EOC cells. It has also been reported[9] that HOTAIR can increase HER-2 expression and enhance the activity of gastric cancer. Some researchers[10,11] have reported the regulatory effect of HOTTIP on the biological processes of various tumors such as breast cancer, colorectal cancer, etc. Unfortunately, lncRNAs are rarely studied in ovarian cancer.

With the increasing amount of clinical data, we have already entered the era of big data. As a

Corresponding Author: Feng Qu, BM; e-mail: Qufeng327968@126.com

cross-discipline in biology and computer science, bioinformatics stimulates the progress of medical biological research[12]. Therefore, it is important to utilize big data in our clinical studies[13]. In this paper, three lncRNA expression profiles were analyzed together to screen out the differentially expressed lncRNAs in EOC and normal ovarian tissues. KCNMA1-AS1 was finally selected for the following experiments.

Patients and Methods

Data Collection and Analysis

The AFFYMETRIX U133 PLUS 2 platform containing 54764 RNA probes has been widely applied in clinical trials. Hence, the AFFYMETRIX U133 PLUS 2 platform was selected as the research object. We first downloaded three expression profiling microarrays (GSE14001[14], GSE38666[15], GSE40595[16]) from the GEO database, and five datasets containing clinical data of EOC (GSE19829[17], GSE26193[18], GSE30161[19], GSE63885[20], GSE18520[21]). The CEL data files were recorded by Affy data. Limma package was used to analyze the differentially expressed genes in the database and the survival function was used for prognostic analysis.

Re-Annotation of LncRNA Probes

To obtain expression data for lncRNAs in the Affymetrix U133 Plus 2.0 microarray, the microarray annotation file was re-annotated. We first downloaded HG-U133 Plus 2.0 annotation file (cvs format, version number 33). Probe sets assigned as an Ref_Seq ID beginning with NR_ (in the RefSeq database, the ID with NR_ corresponded to a non-coding RNA), ensemble gene ID annotated as antisense, processed transcripts, sense_overlapping, non_sense_medited_decay, sense_intronic and lincRNA, and both assigned as ensemble ID and RefSeq ID with NR_ were screened out. Finally, probe sets containing microRNAs, rRNAs and other short RNAs were excluded[22].

Sample Collection

Tissue samples from 60 EOC patients undergoing surgery in the First Affiliated Hospital of Xi'an Medical University for the first time from July 2012 to June 2017 were collected. Patients were pathologically confirmed as malignant EOC. None of them received preoperative chemotherapy or biochemistry. Thirty cases of normal epithelial ovarian tissue samples were selected as controls. This study was approved by the Ethics Committee of The First Affiliated Hospital of Xi'an Medical University and all patients signed informed consent. Resected samples were immediately frozen in liquid nitrogen and preserved at -80°C for the following experiments.

RNA Extraction and Quantitative Real Time-Polymerase Chain Reaction (qRT-PCR)

The total RNA was extracted from tissue samples by TRIzol method (Invitrogen, Carlsbad, CA, USA) and then transcribed into complementary Deoxyribose Nucleic Acid (cDNA) according to the instructions of PrimeScript RT Master Mix (Invitrogen, Carlsbad, CA, USA). Quantitative Real Time-Polymerase Chain Reaction (qRT-PCR) was performed following the instructions of SYBR® Green Master Mix (TaKaRa, Otsu, Shiga, Japan). Primer sequences used in this study were as follows: GAPDH (Glyceraldehyde 3-phosphate dehydrogenase), F: 5′-CACCCACTCCTCCACCTTTG-3′, R: 5′-CCACCACCCTGTTGCTGTAG-3′; KCNMA1-AS1, F: 5′-TCTTTGCTCTCAGCATCGGTG-3′, R: 5′-CCGCAAGCCGAAGTAGAGAAG-3′.

Cell Culture

Human normal ovarian cell line IOSE-386 and ovarian cancer cell lines HO8910, HEY and A2780 were provided by the American Type Culture Collection (ATCC; Manassas, VA, USA). Cells were cultured in DMEM (Dulbecco's Modified Eagle's Medium; Gibco, Grand Island, NY, USA) containing 10% fetal bovine serum (FBS; Gibco, Grand Island, NY, USA), 100 U/mL penicillin and 100 μg/mL streptomycin (Hyclone, South Logan, UT, USA), and incubated in a 5% CO_2 incubator at 37°C.

Cell Transfection

Cells in good growth condition were selected and seeded in the 6-well plates. Cell transfection was performed until the cell confluence was up to 50%-60% according to the instructions of Lipofectamine 2000 (Invitrogen, Carlsbad, CA, USA). The sequence of siRNA was as follows: sense: GCUACGAGAUCAUGAGCCA, antisense: UGGCUCAUGAUCUCGUAGC.

Cell Counting Kit-8 Assay (CCK-8)

Transfected cells were seeded into 96-well plates with 2×10^3 cells per well. 10 μL of Cell Counting Kit-8 solution (CCK-8; Dojindo, Kumamoto, Japan) was added in each well. The absor-

bance at 450 nm of each sample was measured by a microplate reader (Bio-Rad, Hercules, CA, USA).

Transwell Assay

The upper chamber of transwell chamber was previously coated with Matrigel (BD Biosciences, Franklin Lakes, NJ, USA) and maintained in an incubator for 2 h. Briefly, 100 μL of cell supernatant (1×10^6/mL) and 600 μL of DMEM containing 10% FBS were supplied in the upper and bottom chamber, respectively. The transwell chamber was removed after 24 h of incubation, and the non-migrated cells in the chamber were gently wiped off with a cotton swab. The chamber was fixed with methanol for 15 min, washed with PBS (Phosphate-Buffered Saline; Gibco, Grand Island, NY, USA) twice and stained in 1% crystal violet for 30 min. Finally, 5 randomly selected fields were captured for cell counting.

Western Blot

Total protein was extracted from treated cells by radioimmunoprecipitation assay solution (RIPA; Beyotime, Shanghai, China). The protein sample was separated by electrophoresis on 10% SDS-PAGE (sodium dodecyl sulphate-polyacrylamide gel electrophoresis) and then transferred to polyvinylidene difluoride membrane (PVDF; Millipore, Billerica, MA, USA). After non-specific site blockage in skimmed milk, membranes were incubated with primary antibodies at 4°C overnight. The membranes were then washed with TBST (Tris-buffered Saline with Tween 20) at the other day and incubated with secondary antibody for 2 h. The protein blot on the membrane was exposed by chemiluminescence.

Statistical Analysis

The intersection of different data sets was selected by Venn diagram and analyzed by Stata software. Log-Rank was utilized to calculate HR (hazard ratio) and 95% CI (credibility interval). Measurement data were expressed as mean ± standard deviation. Independent-sample *t*-test was used to compare the intergroup differences and chi-square analysis was used to analyze classification data. $p<0.05$ was considered statistically significant.

Results

Overexpressed KCNMA1-AS1 in EOC was Associated with Prognosis

We first downloaded EOC expression data from GEO database, including GSE14001, GSE38666 and GSE40595. In particular, GSE14001 contained 20 ovarian cancer tissues and 3 normal ovarian tissue; GSE38666 contained 25 ovarian cancer tissues and 20 normal tissues; GSE40595 contained 65 ovarian cancer tissues and 8 normal tissues. Limma package was introduced to search for differentially expressed lncRNAs in the three datasets, followed by depicting the corresponding heat maps. As shown in Figure 1, red and green parts represented upregulated

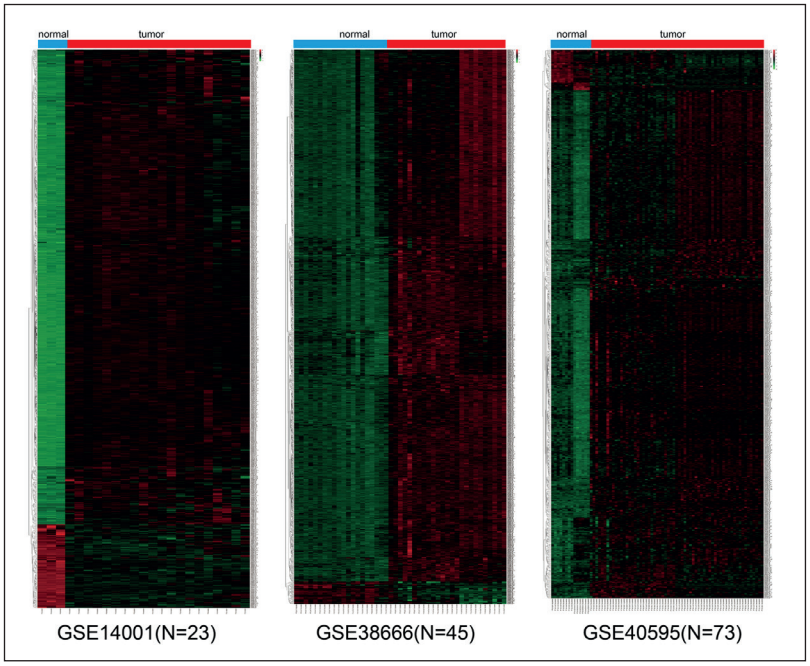

Figure 1. Heat maps of differentially expressed lncRNAs in GSE14001, GSE38666 and GSE40595.

and downregulated lncRNAs in EOC, respectively. A total of 131 upregulated lncRNAs and 4 downregulated lncRNAs were found in the three databases through the Venn diagram. Among them, KCNMA1-AS1 was the most differentially expressed in ovarian cancer tissues than that of normal tissues (Figure 2A-2B).

Subsequently, clinical information of EOC patients and lncRNA expressions in the datasets of GSE19829, GSE26193, GSE30161, GSE63885 and GSE18520 were obtained. The relationship between these lncRNA profiles and prognosis of EOC was analyzed. The results showed that overexpressed KCNMA1-AS1 had no prognostic significance in GSE18520 (p=0.5165, Figure 3A). Moreover, KCNMA1-AS1 was confirmed to be a risk factor for the prognosis of EOC in GSE19829 (p=0.0288), GSE62193 (p=0.0010) and GSE63885 (p=0.0191, Figure 3B, 3C and 3D), which was a good prognostic factor in GSE30161 (p=0.0159, Figure 3E). We then performed the meta-analysis and the results demonstrated that KCNMA1-AS1 expression was negatively correlated to the prognosis of EOC, indicating that KCNMA1-AS1 was a risk factor for EOC (Figure 3F).

Relationship Between KCNMA1-AS1 and Prognosis in Different Types of EOC

Since KCNMA1-AS1 has been proved to be related to the prognosis of EOC, we pathologically divided EOC cases into different subgroups for in-depth analysis. After analyzing the prognostic effect of KCNMA1-AS1 on high-grade EOC, we found that KCNMA1-AS1 was not associated with the prognosis of EOC in GSE18520 (p=0.5156), GSE30161 (p=0.6701) and GSE63885 (p=0.0880, Figure 4A, 4B and 4C). On the contrary, KCNMA1-AS1 was a risk factor for the prognosis of ECO in GSE19829 (p=0.0288) and GSE26193 (p=0.0106, Figure 4D and 4E). Subsequently, meta-analysis also elucidated that KCNMA1-AS1 was a risk factor in the prognosis of high-grade EOC (Figure 4F).

We next analyzed the prognostic role of KCNMA1-AS1 in advanced EOC. The data showed that KCNMA1-AS1 had no prognostic significance in GSE18520 (p=0.5156) and GSE30161 (p=0.2940, Figure 5A and 5B). However, KCNMA1-AS1 was proved to be a risk factor for prognosis of EOC in GSE26193 (p=0.0220), GSE19829 (p=0.0361) and GSE63885 (p=0.0275; Figure 5C-5E). The meta-analysis suggested that KCNMA1-AS1 was a risk factor for the prognosis of advanced EOC (Figure 5F).

EOC is pathologically divided into serous, mucinous, endometrioid and other subtypes, of which serous epithelial ovarian cancer is the most common one. In serous EOC, KCNMA1-AS1 had no prognostic significance in GSE18520 (p=0.5156), GSE30161 (p=0.6646) and GSE26193 (p=0.1221; Figure 6A-6C). However, KCNMA1-AS1 was a risk factor for prognosis of EOC in GSE19829 (p=0.0288) and GSE63885 (p=0.0090, Figure 6D and 6E). The meta-analysis found that KCNMA1-AS1 was a prognostic risk factor in serous EOC (Figure 6F).

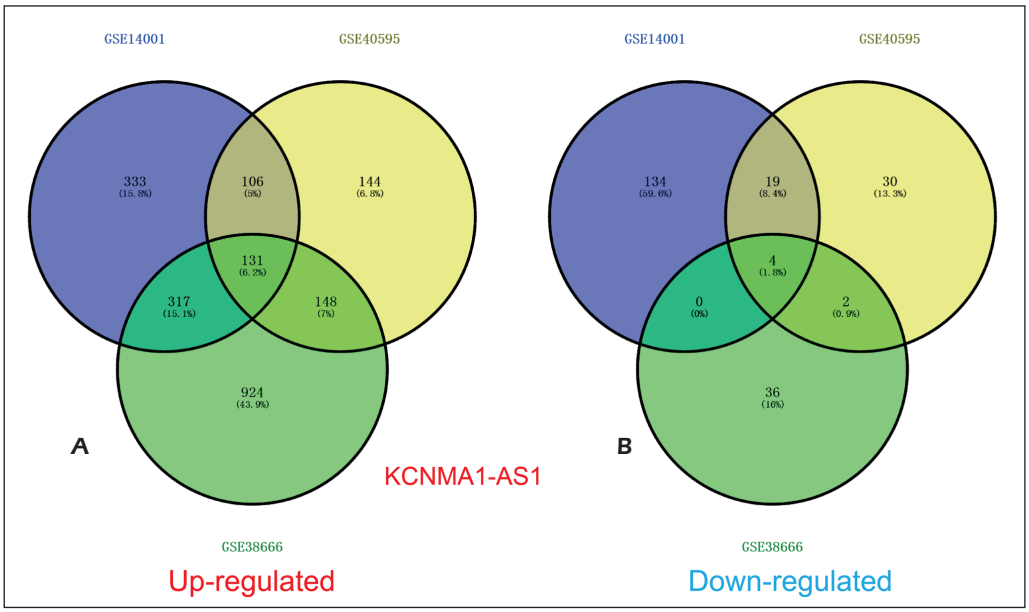

Figure 2. Upregulated **A**, and downregulated **B**, lncRNAs expressed in GSE14001, GSE38666 and GSE40595.

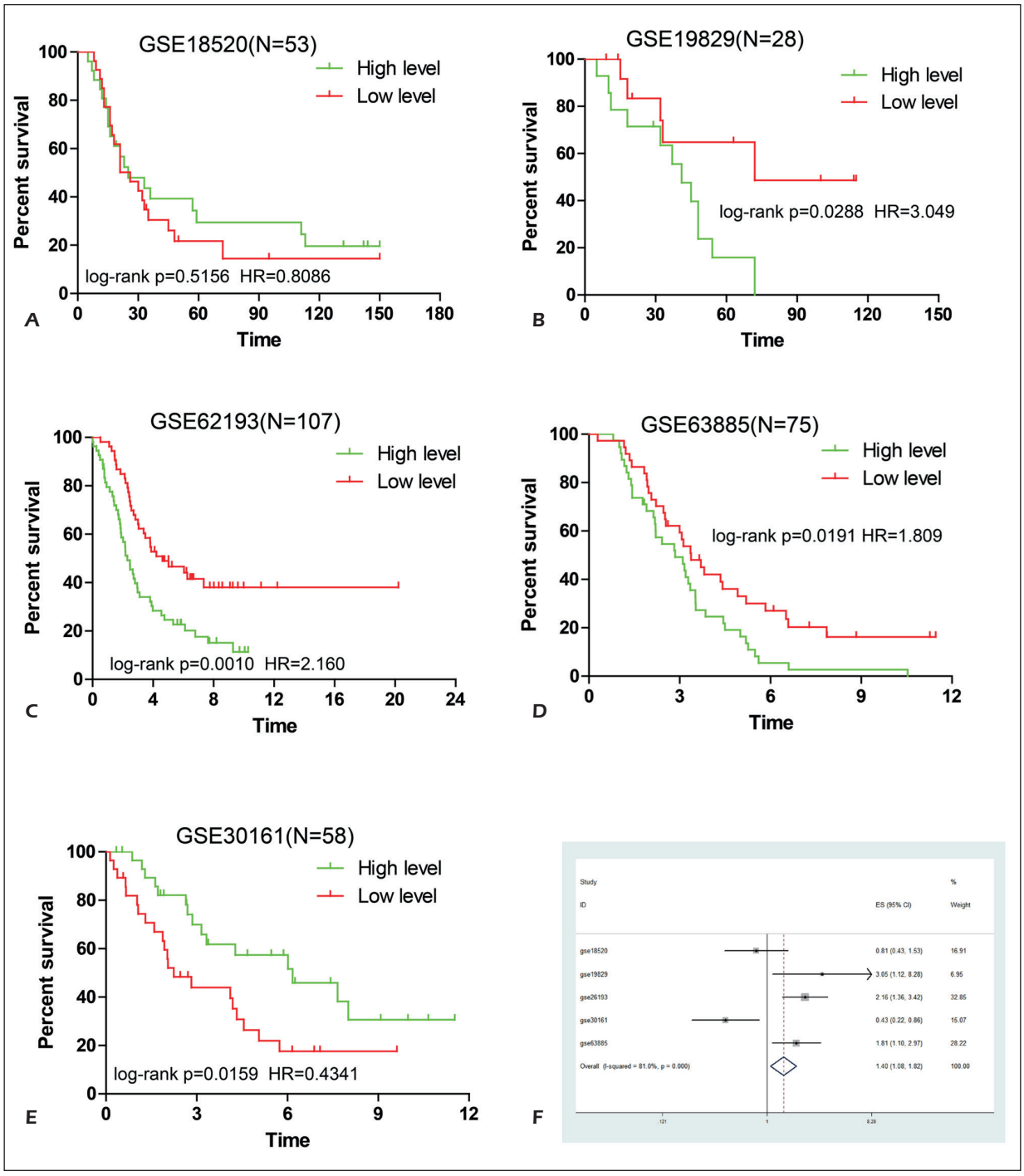

Figure 3. KCNMA1-AS1 was a risk factor for the prognosis of epithelial ovarian cancer. **A**, KCNMA1-AS1 had no prognostic significance in GSE18520. **B**-**D**, KCNMA1-AS1 was a risk factor for the prognosis in GSE19829 **B**, GSE62193 **C**, and GSE63885 **D**. **E**, KCNMA1-AS1 was a good prognostic factor in GSE30161. **F**, KCNMA1-AS1 was a risk factor for the prognosis of epithelial ovarian cancer.

KCNMA1-AS1 was a prognostic risk factor in high-grade, advanced and serous EOC. The higher the expression level of KCNMA1-AS1, the worse the prognosis of EOC patients.

KCNMA1-AS1 was Upregulated in Ovarian Cancer Tissues

KCNMA1-AS1 expression in 60 ovarian cancer tissues and 30 normal ovarian tissues was detect-

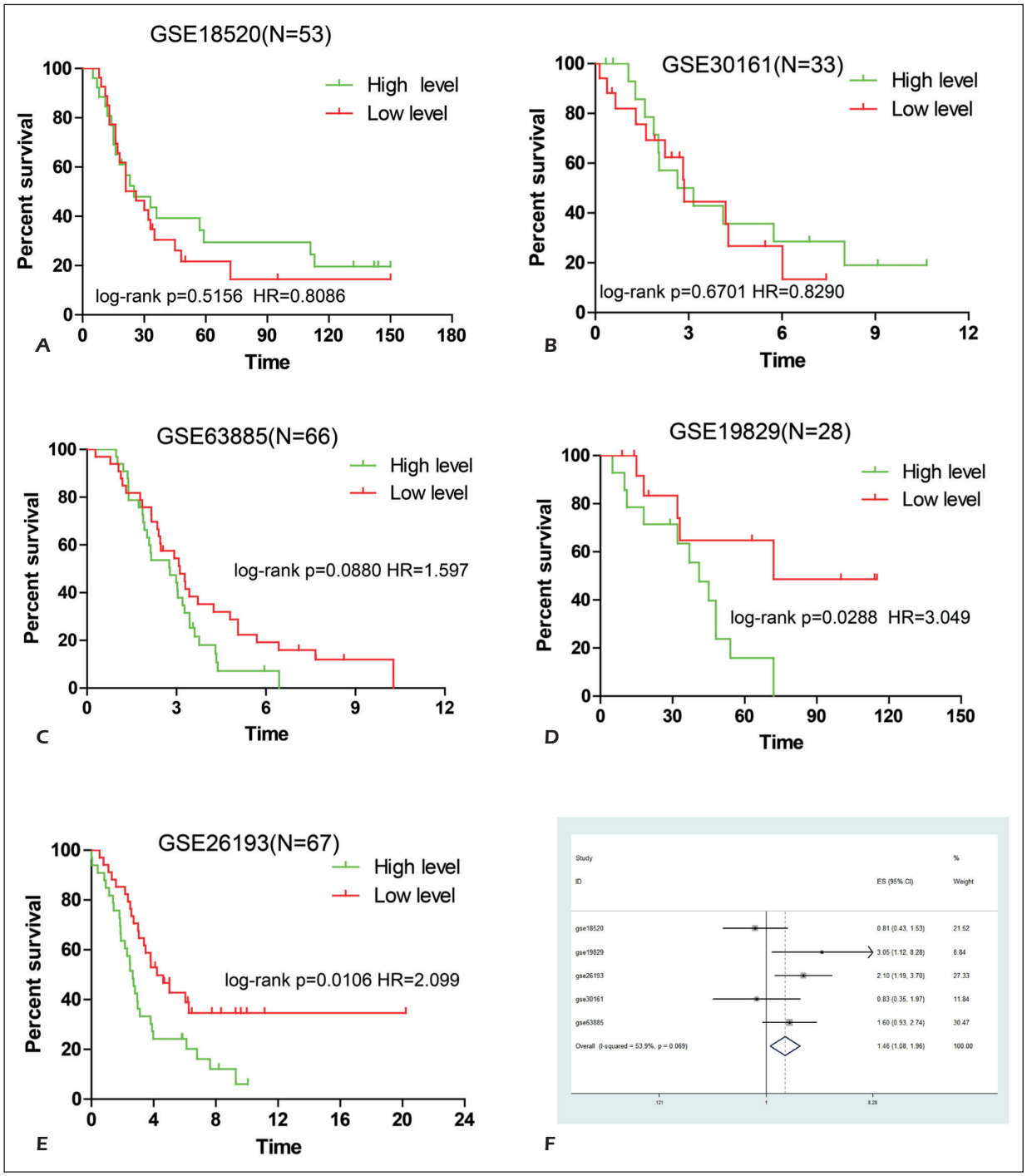

Figure 4. KCNMA1-AS1 was a prognostic risk factor for high-grade epithelial ovari-an cancer. **A-C**, KCNMA1-AS1 had no prognostic significance in GSE18520, GSE30161 and GSE63885. **D-E**, KCNMA1-AS1 was a risk factor for prognosis in GSE19829 and GSE26193. **F**, KCNMA1-AS1 was a prognostic risk factor for high-grade epithelial ovarian cancer.

ed by qRT-PCR. The results indicated a higher expression of KCNMA1-AS1 in ovarian cancer than that of normal ovarian tissues (p<0.001, Figure 7A). EOC patients were further assigned into the high-expression group and low-expression group based on their relative level of KCNMA1-AS1 in ovarian cancer tissues. Lower DFS and OS were observed in EOC patients with high-level KCNMA1-AS1 than those with low-level (p=0.0264, p=0.0244, Figure 7B and 7C).

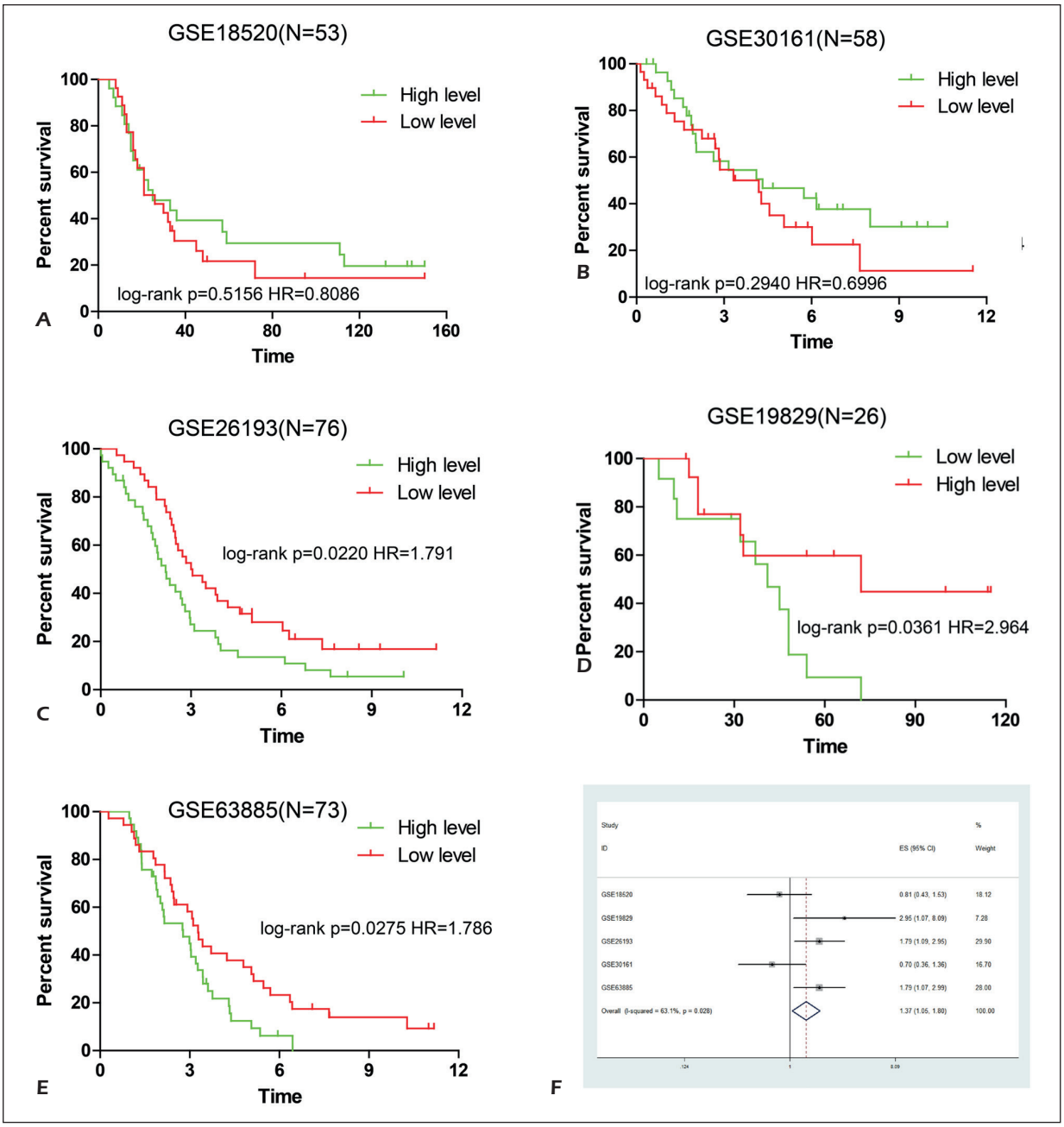

Figure 5. KCNMA1-AS1 was a prognostic risk factor for advanced epithelial ovarian cancer. **A**-**B**, KCNMA1-AS1 had no prognostic significance in GSE18520 and GSE30161. **C**-**E**, KCNMA1-AS1 was a risk factor for the prognosis in GSE62193, GSE19829 and GSE63885. **F**, KCNMA1-AS1 was a prognostic risk factor for ad-vanced epithelial ovarian cancer.

ROC curve was introduced based on the expression of KCNMA1-AS1, and the data showed that KCNMA1-AS1 had a certain diagnostic value (Figure 7D). These results suggested that KCNMA1-AS1 may be involved in the development of EOC.

Overexpressed KCNMA1-AS1 Promoted Proliferation and Migration of Ovarian Cancer Cells

To investigate the effect of KCNMA1-AS1 on ovarian cancer cells, we first detected KCNMA1-AS1 expression in ovarian cancer cells

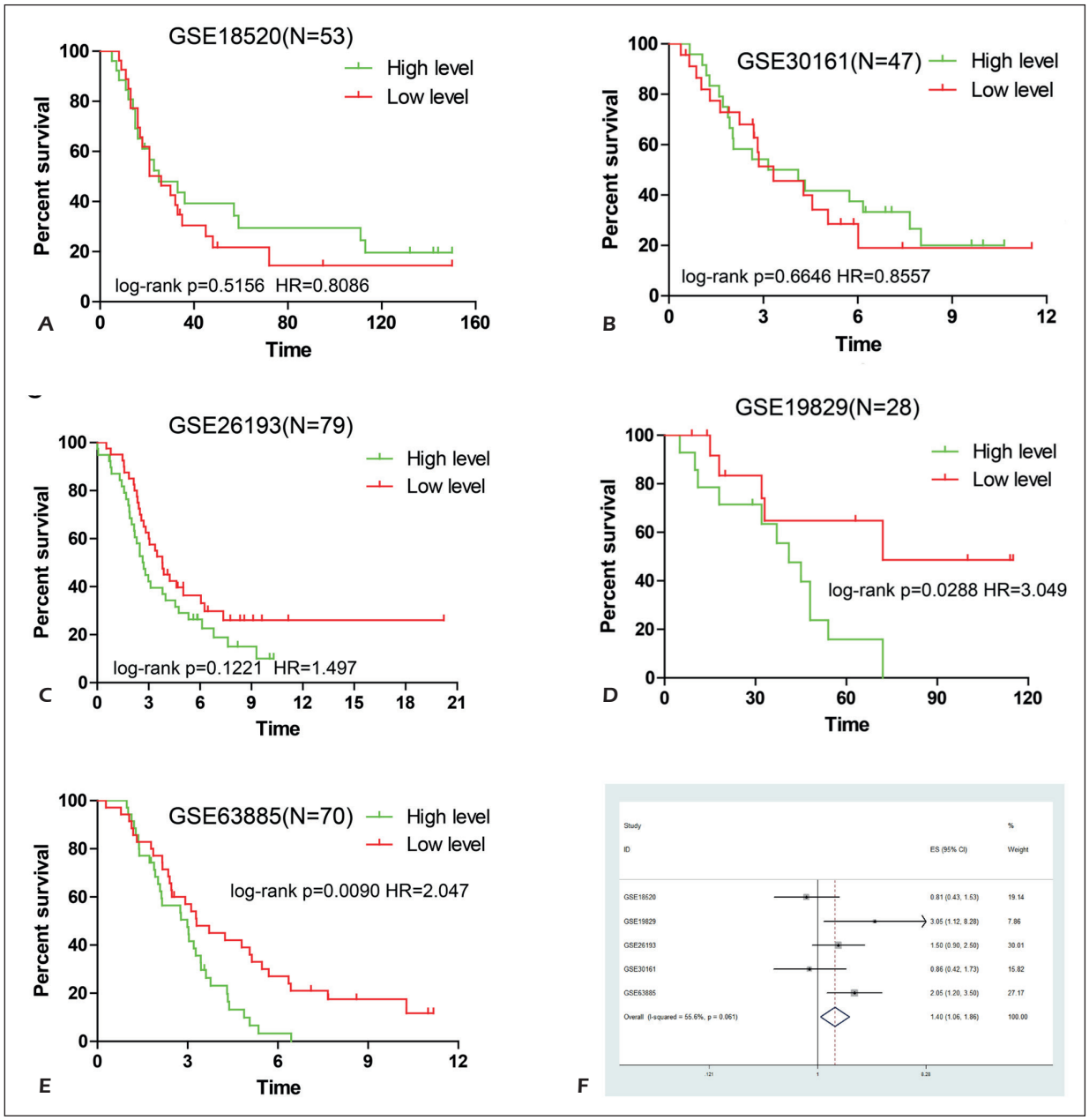

Figure 6. KCNMA1-AS1 was a prognostic risk factor for serous epithelial ovarian cancer. **A-C**, KCNMA1-AS1 had no prognostic significance in GSE18520, GSE30161 and GSE26193. **D-E**, KCNMA1-AS1 was a risk factor for the prognosis in GSE19829 and GSE63885. **F**, KCNMA1-AS1 was a prognostic risk factor for se-rous epithelial ovarian cancer.

(HO8910, HEY and A2780) and normal ovarian cell strain (IOSE-386) by qRT-PCR. Higher expression of KCNMA1-AS1 was observed in ovarian cancer cells than that of normal ovarian cells (Figure 8A). Besides, HO8910 cells were selected for the following cell experiments since they presented the highest expression of KCNMA1-AS1. Subsequently, HO8910 cells were transfected with si-KCNMA1-AS11, si-KCNMA1-AS12 or overexpression plasmids, respectively. Transfection efficacy was validated by qRT-PCR (Figure 8B-8C). We then carried out CCK-8 and transwell assay for evaluating the regulatory effects of KCNMA1-AS1 on proliferation and migration of ovarian cancer cells, respectively. Cell proliferation was detected after transfection for 6, 24, 48, 72 and 96 h, respectively. The results showed a remarkable decrease in the proliferative ability after transfection with

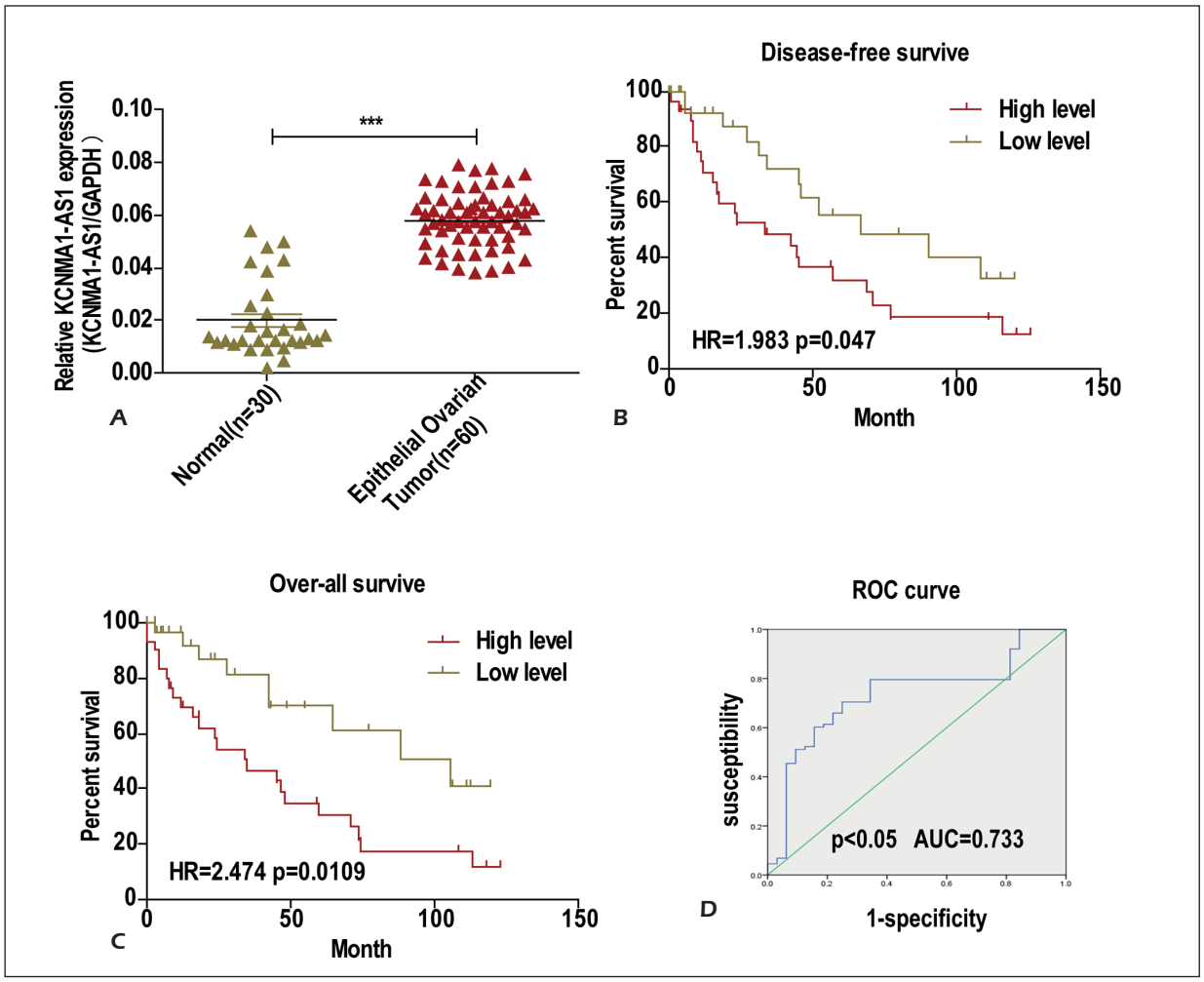

Figure 7. KCNMA1-AS1 was overexpressed in epithelial ovarian cancer. **A**, KCNMA1-AS1 was overexpressed in epithelial ovarian tissues of 60 patients with epithelial ovarian cancer than that of 30 controls. **B**, Disease-free survival of epithelial ovarian cancer patients with higher expression of KCNMA1-AS1 was significantly lower than those with lower expression. **C**, Overall survival rate of epithelial ovarian cancer patients with higher expression of KCNMA1-AS1 was significantly lower than those with lower expression. **D**, ROC curve ofKCNMA1-AS1 expression and diagnostic sensitivity of epithelial ovarian cancer.

si-KCNMA1-AS1 2 in ovarian cancer cells (Figure 8D-8F). The transwell assay obtained similar results (Figure 8G), indicating that overexpressed KCNMA1-AS1 promoted proliferation and migration of ovarian cancer cells.

KCNMA1-AS1 Participated in the Development of EOC by Regulating the Apoptosis Pathway in HO8910 Cells

Apoptosis was remarkably induced after transfection with si-KCNMA1-AS1 in ovarian cancer cells (Figure 9A and 9B). Moreover, the expressions of activated Caspase-3 and Caspase-9 were elevated after KCNMA1-AS1 knockdown (Figure 9C and 9D). Bcl-xL has a significant anti-apoptotic effect. The data also elucidated that Bcl-xL expression remarkably decreased after transfection with si-KCNMA1-AS1 (Figure 9C and 9D), suggesting that KCNMA1-AS1 participated in the development of EOC by regulating cell apoptosis.

Discussion

Epithelial ovarian cancer is the most common type of ovarian cancer. The mortality of EOC is up to 50% and the 5-year survival rate is only about 30%. Symptoms are occult in the early-stage EOC since the ovaries exist in the deep pelvic cavity. EOC patients are usually in an ad-

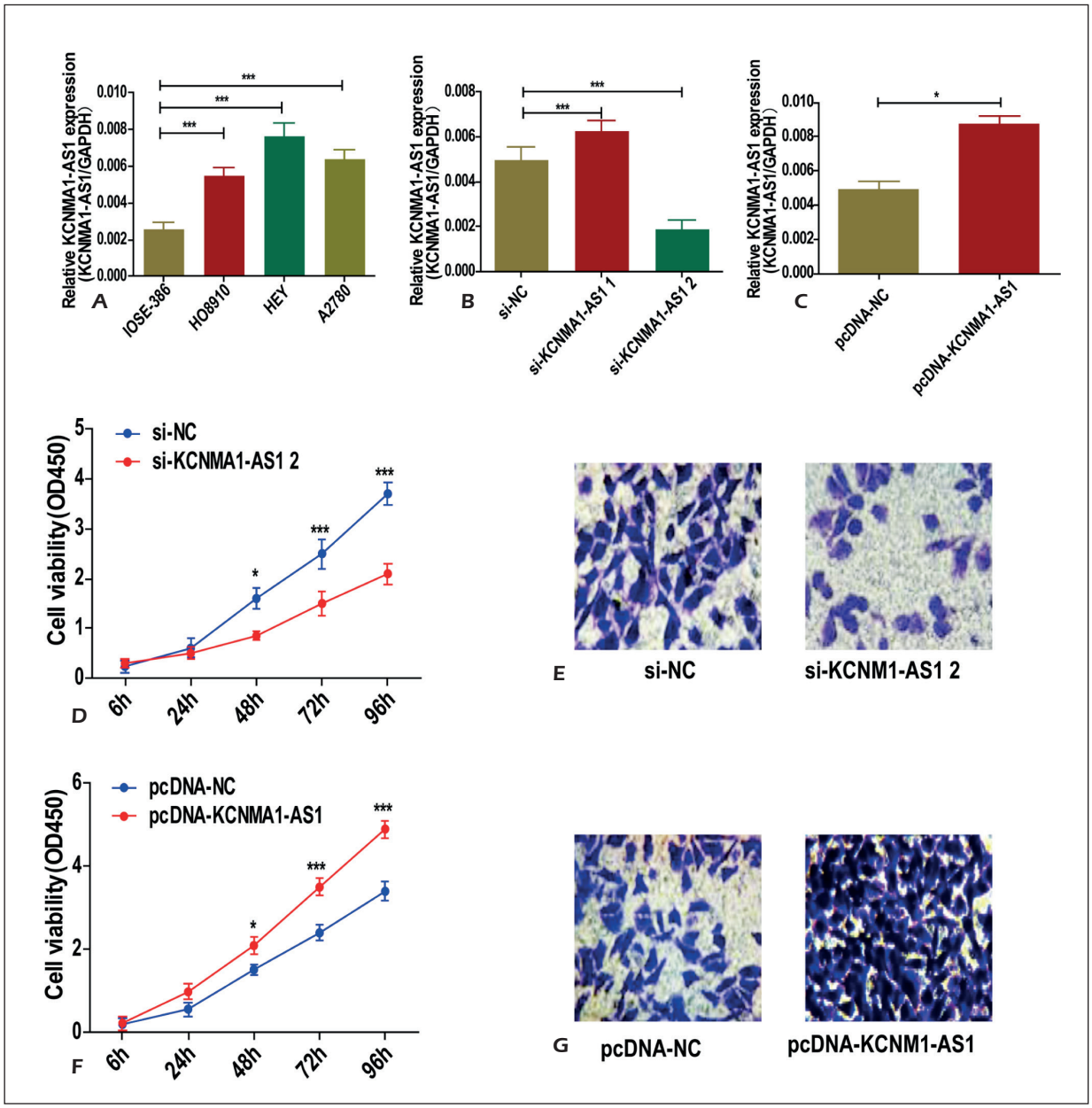

Figure 8. Overexpressed KCNMA1-AS1 promoted proliferation of epithelial ovarian cells. ***A***, The expression levels of KCNMA1-AS1 in ovarian normal cell line (IOSE-386) and ovarian cancer cell lines (HO8910, HEY, A2780). ***B***, ***C***, Transfection efficacy after KCNMA1-AS1 interference ***B***, or overexpression ***C***, in HO8910 cells. ***D***, Cell viability was decreased after KCNMA1-AS1 knockdown. ***E***, Cell migration was de-creased after KCNMA1-AS1 knockdown (magnification: 40×). ***F***, Cell viability was increased after KCNMA1-AS1 overexpression. ***G***, Cell migration was increased after KCNMA1-AS1 overexpression (magnification: 40×)

vanced stage at the firsts time of diagnosis. Extensive planting and metastasis in the pelvic cavity and abdominal cavity could rapidly appeared in a very short time[23]. Lack of effective treatments, easy relapse and non-susceptibility to chemotherapy all lead to the poor diagnosis of EOC[24]. It is urgent to investigate the molecular mechanism of EOC, to provide new directions for prevention, diagnosis and treatment of ovarian cancer.

In recent years, a large number of studies have demonstrated that lncRNA exerts an important role in tumor development. For example, HOTAIR can regulate the cell cycle in gliomas, which is also a risk factor for the prognosis of gliomas[25]. HOXA11-AS can inhibit downstream tumor-suppressor genes by binding to PRC2, LSD1 and DNMT1, resulting in an increased tumor activity[26]. MEG3 is a prognostic risk factor in cervical

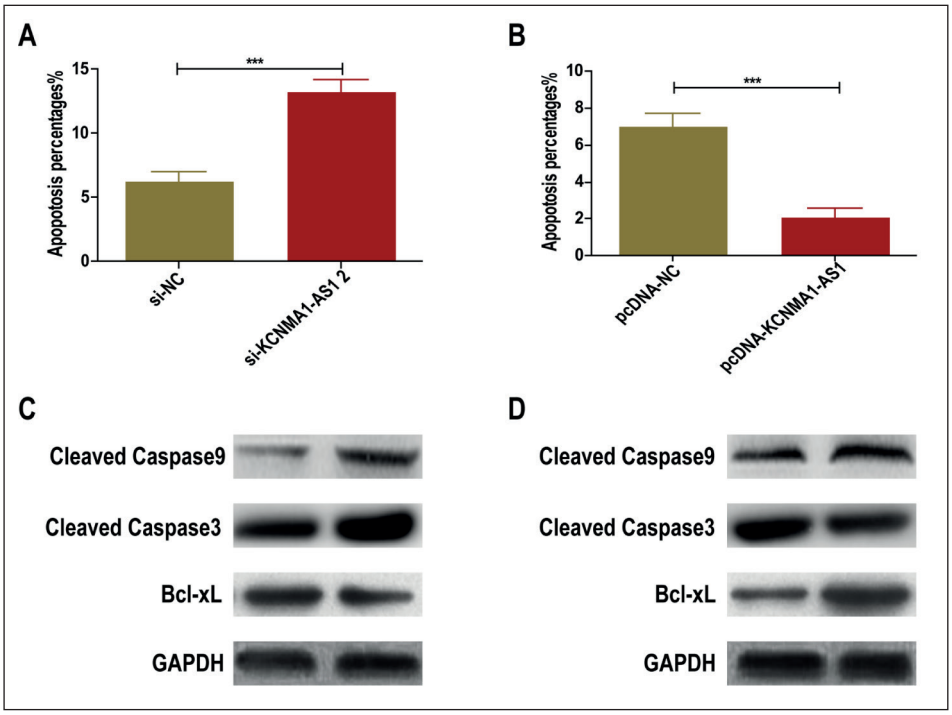

Figure 9. KCNMA1-AS1 participates in the development of epithelial ovarian cancer by regulating apoptosis of HO8910 cells. **A**, Cell apoptosis was increased after KCNMA1-AS1 knockdown. **B**, Cell apoptosis was decreased after KCNMA1-AS1 overexpression. **C**, Protein expressions of apoptosis-related factors after KCNMA1-AS1 knockdown. **D**, Protein expressions of apoptosis-related factors after KCNMA1-AS1 overexpression.

cancer[27]. The role of various lncRNAs in ovarian cancer, however, remains unknown. Therefore, it is of great significance to investigate the effect of lncRNA on ovarian cancer. In this work, differentially expressed KCNMA1-AS1 was obtained by analyzing the GEO database for lncRNA expression in EOC. Meta-analysis showed that KCNMA1-AS1 may be a prognostic risk factor for EOC. We next validated KCNMA1-AS1 expression in EOC patients and analyzed its relationship with prognosis, which was consistent with the results analyzed in the GEO database. Overexpressed KCNMA1-AS1 was proved to be able to promote proliferation and migration of ovarian cancer cells.

Apoptosis is a programmed cell death process, which is strictly controlled by some certain apoptotic-related genes. In normal human tissues, apoptosis contributes to eliminating aging cells and abnormal cells, thus maintaining the body's homeostasis to better adapt to the environment. In contrast, tumor cells present an uncontrolled growth condition, abnormal proliferation and inhibited apoptosis. Common anti-apoptotic genes (Bcl-2, Bcl-xL, etc.,) and pro-apoptotic genes (Bax, Bad, Bid, etc.,) are often active in tumor cells[28]. BcI-xL is one of the significant members of the Bcl-2 gene family, which is involved in various protein-protein interactions and exerts anti-apoptotic function[29]. It is generally believed that Bcl-xL function is similar to that of Bcl-2. However, the specific roles of both Bcl-xL and Bcl-2 are varied in different cell types and apoptotic signaling pathways. So far, Bcl-xL is found to be widely expressed in tumors, which is highly expressed in most central nervous system tumors than that of Bcl-2[30].

In addition, Caspase is the mediator and executor of cell apoptosis. Studies have shown that cell apoptosis is caused by the gradual cascade reaction of Caspase. In particular, Caspase-3 is the downstream factor in the Caspase cascade and considered to be the actual implementer of apoptosis induction. It is reported that the expressions and activities of Caspase-3 and Caspase-9 upregulate after cell apoptosis[31]. Typically, there are two classic apoptotic pathways, including extracellular and intracellular apoptotic pathways. In the extracellular pathway, the death ligand binds to the corresponding receptor to form a death signal, which in turn stimulates the signaling molecule and further binds to Caspase-8. After the formation of the death-inducing signaling complex, Caspase-8 and Caspase-3 are further activated to induce cell apoptosis. On the other hand, the intracellular pathway is also known as the mitochondrial pathway. A polycomplex is formed by apoptotic protease-activating factor-1 and apoptotic factors after activation of the intracellular

pathway of Caspase. Cytosolic Caspase-9 precursor subsequently binds to the polycomplex to further stimulate Caspase-3, thereafter inducing cell apoptosis[32]. In this study, we found increased Bcl-xL expression, and decreased activities of Caspase-3 and Caspase-9 after KCNMA1-AS1 overexpression, suggesting that KCNMA1-AS1 could inhibit apoptosis of ovarian cancer cells.

Conclusions

We found that KCNMA1-AS1 is overexpressed in epithelial ovarian cancer and negatively correlated with its prognosis. KCNMA1-AS1 participates in the occurrence and development of epithelial ovarian cancer by promoting proliferation, migration and inhibiting apoptosis of ovarian cancer cells *via* apoptosis pathway.

Conflict of Interests

The authors declared no conflict of interest.

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