Disulfidptosis-related prognostic model based on multiomics and the significance of IL1B in ovarian cancer

Kunyu Wang
National Cancer Center, Chinese Academy of Medical Sciences and Peking Union Medical College

Bin Li (libin@cicams.ac.cn)
National Cancer Center, Chinese Academy of Medical Sciences and Peking Union Medical College

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Abstract

Background

Ovarian cancer (OC) is a significant health concern for women due to high mortality rates. Disulfidptosis is a newly discovered mechanism of caspase-driven programmed cell death that may be significant for cancer treatment.

Methods

The bulk RNA-seq data of 378 OC patients in TCGA-OV cohort and 174 patients in GSE53963 dataset, and the single-cell RNA-seq data of 4 high-grade SOC patients in GSE154600 were retrieved. The disulfidptosis score was calculated by gene set enrichment analysis (GSEA) based on the disulfidptosis pathway using the AddModuleScore function of the Seurat package. The patients were divided into the two groups based on the risk score, which were then compared using consensus clustering, WCGNA and functional enrichment analysis. LASSO regression and cox regression were performed to construct a risk score model. Immune cell infiltration was analyzed by xcell and ssGSEA. IL1B was knocked down in OC cell lines, and routine in vitro and in vivo functional assays were performed.

Results

We identified 6 cell clusters in OC and divided them on the basis of the disulfidptosis score. The two groups showed distinct functional difference. Likewise, OC patients divided into disulfidptosis score-related groups showed significant difference in survival status, along with enrichment of immune response-related pathways. Seven prognostic genes related to disulfidptosis were screened by Cox regression and LASSO regression analyses, and the risk score was calculated. The high-risk score was associated with significantly worse survival in the validation cohort. In addition, the abundance of activated T cells was higher, and that of Tregs and MDSCs were lower in the low-risk group compared to the high-risk group. Finally, IL1B silencing inhibited the proliferation, migration, and invasion of OC cells in vitro and in vivo.

Conclusion

The disulfidptosis-based risk model can accurately predict the prognosis and immune characteristics of OC patients. IL1B functions as an oncogene in OC, and is a promising therapeutic target.

1 Introduction

Ovarian cancer (OC) is the fourth most frequent and third most lethal malignancy among females worldwide [1]. Around 55,342 new OC cases and 37.519 deaths were recorded in China in 2020, which respectively accounted for about 18% of the global cases of OC and 18.1% of OC-related mortality [2, 3]. Given the lack of effective screening measures and specific clinical symptoms, the onset of OC is frequently insidious. In fact, approximately 70–75% of the cases diagnosed at an advanced stage [4], resulting in a dismal 5-year overall survival (OS) rate of less than 50% [5]. Therefore, it is critical to identify novel therapeutic targets and prognostic markers for OC in order to improve both recurrence-free survival (RFS) and OS.
Disulfdptosis is a newly discovered mechanism of caspase-driven programmed cell death that is closely associated with the actin cytoskeleton, which is vital for the maintenance of cell shape and survival. SLC7A11, a member of the SLC family, protects cells against oxidative stress by maintaining intracellular glutathione levels [6] [7]. It rapidly reduces cystine to cysteine, a process that requires large amounts of NADPH from the glucose-pentose phosphate pathway (PPP), resulting in significant depletion of cellular NADPH pools [7]. Therefore, restricted glucose supply or impaired redox homeostasis can lead to the accumulation of cystine or other disulfide molecules, resulting in the formation of abnormal disulfide bonds between actin proteins, eventually leading to the collapse of the cytoskeleton and inducing disulfide stress-induced cell death [8].

The disulfide stress-induced cell death or disulfidptosis is a potential new therapeutic target in cancer therapy [8]. Ferroptosis, a form of regulated cell death induced by excessive lipid peroxidation, is a key tumor suppression mechanism [9–12], and recent studies have shown that activating ferroptosis and apoptosis can inhibit OC progression [13, 14]. Agrimonolide induces apoptosis and ferroptosis in OC cells by targeting SCD1, and is a promising therapeutic agent for OC [15]. Furthermore, combined application of cisplatin and a RUNX1 inhibitor can augment apoptosis in OC cells [16]. Although most chemotherapy drugs activate the apoptotic cascade in cancer cells, the latter have evolved mechanisms to evade apoptosis, resulting in therapy resistance and relapse. Therefore, targeting disulfide stress-induced death can be a promising alternative target for the treatment of OC and other cancers.

In our study, we established a disulfidptosis score and accordingly divided the cell types in SOC patients into subgroups with distinct features, especially in cell communication. Furthermore, 7 disulfidptosis-related genes of prognostic significance were used to construct a risk score-based predictive model. The patients stratified on the basis of this risk score displayed significant differences in prognosis and immune infiltration profile. IL1B had the highest risk coefficient in the risk score model, and was further confirmed as an oncogene through functional assays. Our findings provide novel insights into the mechanisms underlying the progression of OC.

2 Methods

2.1 Data acquisition

The gene expression data and corresponding clinical data of OC patients were retrieved from TCGA and GEO databases. TCGA-OV dataset includes bulk RNA-seq data of 378 OC patients, and the GSE53963 dataset includes bulk RNA-seq of 174 OC patients. The single-cell RNA-seq data of 5 high-grade SOC patients was retrieved from the GSE154600 dataset.

2.2 Single cell sequencing data processing and analysis

The single cell sequencing data was subjected to dimensionality reduction, and the cell were divided into 6 populations. The GSVA enrichment pathway scores of these populations were calculated using 50 Hallmark datasets. The disulfidptosis score was obtained by gene set enrichment scoring of the disulfidptosis pathway using the AddModuleScore function of the Seruat package. Each immune cell group was divided into disulfidptosis<sub>high</sub> and disulfidptosis<sub>low</sub> groups based on the score. Cell Chat analysis was performed to assess cell communication, and the scores were calculated by dividing the 12 immune cell subsets on the basis of the disulfidptosis score. The gene set score of Hallmark pathways was scored by GSVA.

2.3 Screening of differentially expressed genes (DEGs)
The DEGs between the disulfidptosis\textsuperscript{high} and disulfidptosis\textsuperscript{low} groups were screened using the FindAllmarkers function of the Seruat package, with adjusted P value threshold of 0.585.

2.4 Consensus clustering analysis

Consensus clustering was performed using the R package ConsensusClusterPlus. The number of iterations was set to 500, clustering method to k-means clustering, and the distance parameter to Euclidean distance. The number of clusters was evaluated by the CDF curve. The OC patients were accordingly divided into clusters C1 and C2.

2.5 Weighted correlation network analysis (WCGNA)

Four modules were identified by WCGNA algorithm, and the module with the closest correlation with C1 and C2 was selected.

2.6 Functional enrichment analysis

GO analysis was performed on the 122 genes in the selected module using the R package clusterProfiler (version 4.0.5). False discovery rate (FDR) less than 0.05 was set as the threshold for significance.

2.7 Lasso regression model

Lasso regression analysis was performed to screen for the prognostic genes in the TCGA-OV cohort. The risk score was calculated as follows:

\[
\text{riskscore} = \text{Coef}_1 \times \text{Geneexpression}_1 \times \text{Coef}_2 \times \text{Geneexpression}_2 \times \cdots \times \text{Coef}_n \times \text{Geneexpression}_n
\]

According to the median risk score, the patients in TCGA-OV and GSE53963 cohorts were divided into the high-risk and low-risk groups. Survival curves were plotted and analyzed by the Kaplan-Meier method.

2.8 Immune cell infiltration analysis

The immune infiltration score was calculated using the ssGSEA and xCell algorithms, and were visualized by box plot, heat map and scatter plot. The enrichment scores of single sample and gene set pairing were calculated by ssGSEA to determine the degree of immune infiltration. The xCell algorithm was used to quantify the abundance of 67 immune cell types using transcriptome data.

2.9 Mutation analysis

The TCGA-OV mutation data was analyzed using the R package maftools (version 2.12.0).

2.10 Cell culture and lentivirus packaging

The 293T and SKOV3 cell lines were purchased from the American Type Culture Collection (ATCC; Manassas, VA, USA), and A2780 cells were obtained from the National Experimental Cell Resource Sharing Platform (Beijing, China). The 293T cells were cultured in DMEM supplemented with 10% fetal bovine serum (FBS), SKOV3 cells in McCoy’s 5A supplemented with 10% FBS, and A2780 cell line in RPMI 1640 supplemented with 10% FBS.

To produce pSIH-puro lentiviruses, the packaging plasmids vSVG, pLP1 and pLP2 and lentiviral vectors were co-transfected into HEK293T cells. After 48 h, the supernatant was collected and stored in aliquots at -80°C. For lentivirus infection, cells were first treated with polybrene (5µg/mL) (TR-1003, Sigma) and then incubated with the specific lentiviruses. Stable transduced cell lines were selected by culturing in the presence of puromycin (2µg/mL)
(540222, Sigma) for 2 weeks. The IL1B shRNA sequences were as follows (5'-3'): sh1, CGGCCAGGATATAACTGACTT and sh2, GCGATTTGTCTTCAACAAGAT.

2.11 CCK-8 assay

OVC cells were seeded in 96-well plates at the density of 2×10^3 cells/well and cultured for 5 days. At pre-selected time points, CCK-8 reagent (Targetmol) was added to each well at 1:10 dilution, and the cells were incubated for 1h. The absorbance of each well was measured at 450 nm (OD\textsubscript{450}), and the relative cell proliferation rate was calculated by normalizing the OD\textsubscript{450} on days 2–5 to that of day 1. To assess cell viability, the OV cells were seeded in 96-well plates at the density of 1×10^4 cells/well, and the absorbance at 450 nm was measured 24h later as described. Cell viability was calculated by normalizing OD\textsubscript{450} of the experimental groups to that of the negative control group.

2.12 Colony forming assay

SKOV3 and A2780 cells were seeded in 6-well plates at the density of 1.5 x 10^3 cells/well, and cultured for 9–12 days until visible colonies appeared. The wells were washed with PBS, and the colonies were fixed with methanol for 15 minutes, stained with crystal violet, and counted under a microscope.

2.13 Western blotting

The suitably treated cells were harvested and lysed with RIPA buffer (1% NP-40, 0.1% sodium dodecyl sulfate (SDS), 50 mM Tris–HCl pH 7.4, 150 mM NaCl, 0.5% sodium deoxycholate, 1 mM (EDTA), 1×proteinase inhibitor cocktail (Roche)) for 30 min on ice. The proteins were resolved by 10% SDS-PAGE and transferred onto PVDF membranes (Millipore). After blocking with 5% skim milk, the membranes were incubated overnight with anti-IL1B (1:1000; ab283818, Abcam) and anti-β-actin (1:4000; Abclonal) antibodies at 4°C. Following incubation with secondary antibodies, the immunoblots were visualized using the ImageQuant LAS-4000 System (GE).

2.14 Transwell assay

Parental SKOV3 (4 × 10^4 per insert) or A2780 cells (6 × 10^4 per insert) were suspended in FBS-free RPMI 1640 and seeded into the upper chambers with or without Matrigel (BD, Franklin Lakes, NJ, USA) pre-coating. The bottom chambers were filled with 10% FBS-supplemented RPMI 1640 medium. After 24 h incubation, the migratory or invasive cells were fixed with methanol and stained with crystal violet. The number of cells were counted in three randomly selected fields and statistically analyzed.

2.15 Animal experiments

All animal experiments were approved by the Animal Care and Use Committee of the Chinese Academy of Medical Sciences Cancer Hospital. To induce metastatic growth \textit{in vivo}, luciferase-labeled A2780 cells transfected with shIL1B or the empty vector were intraperitoneally injected into 6-weeks-old female BALB/c nude mice (1×10^6 cells/mouse). After 18 days, the luciferase signals were measured. Once the tumors had grown for the stipulated duration, the mice were euthanized and the tumors were harvested.

2.16 Statistical analysis

All statistical analyses are performed using R. Univariate and multivariate Cox regression were performed by the R package survival and survminer, and p value < 0.05 was considered statistically significant.
3 Results

3.1 Characterization of cell types by disulfidptosis-related score

The single cell sequencing data of 4 high grade SOC cases was retrieved from the GSE154600 dataset, and subjected to dimensionality reduction. The cells were divided into 6 populations (Fig. 1A), and the proportion of each cell type in the 4 cases is shown in Fig. 1B. The AddModuleScore function was used to determine the disulfidptosis score of each population by calculating the gene set enrichment score of the disulfidptosis pathway. Accordingly, each immune cell group was divided into the disulfidptosis\(_{\text{high}}\) and disulfidptosis\(_{\text{low}}\) groups (Fig. 1C). The disulfidptosis gene set-related scores of each cell type are shown in Fig. 1D, and the proportion of the different cell populations in each patient is shown in Fig. 1E. The immune cell subsets were identified using specific marker genes. For instance, LUM, COL3A1 and DCN were the markers for fibroblasts, and LYZ, C1QB and CD68 were used for myeloid cells (Fig. 1F). Cell chat analysis was performed to determine whether difference in the disulfidptosis score in the same cell type affected cell-to-cell communication (Fig. 2A). The interaction intensity was calculated in the 12 immune cell subsets divided by the disulfidptosis score. Regardless of their disulfidptosis score, the fibroblasts interacted strongly with the endothelial cells with high disulfidptosis score. Furthermore, the disulfidptosis score had little effect on the interaction between myeloid cells and endothelial cells. The disulfidptosis\(_{\text{high}}\) epithelial cells showed significantly higher interaction with the fibroblasts compared to the disulfidptosis\(_{\text{low}}\) counterparts. These results suggested the disulfidptosis might regulate the interaction of fibroblasts with epithelial and endothelial cells in the ovarian TME. We next performed GSVA to gauge the gene set score of Hallmark pathways. As shown in Fig. 2B, the endothelial cells were highly enriched in the Wnt-\(\beta\)-catenin and TGF-\(\beta\) signaling pathways, and myeloid cells were enriched in the IFN-\(\gamma\) and IFN-\(\alpha\) pathways. As expected, the Myc pathway was enriched in the epithelial cells.

3.2 Functional difference analysis by WCGNA and GO analysis

Through consensus clustering, 378 OC patients from TCGA-OV cohort were divided into C1 and C2 clusters (Fig. 3A-B), which differed significantly in terms of prognosis (Fig. 3C). The number of clusters was evaluated by the CDF curve (Fig. 3D, E). Principal component analysis (PCA) that the two clusters were distinct (Fig. 3F). Weighted gene co-expression network analysis (WCGNA) identified 4 gene modules, and the module with the strongest correlation with C1 and C2 consisted of 122 genes (Fig. 4A-C). GO analysis was performed to characterize the functional difference in the two groups, with FDR of 0.05 as the threshold for significance. The significantly enriched biological processes (BP) were humoral immune response and activation of immune response. In addition, multiple terms of external side of membrane were enriched for cell components (CC), and cytokine activity was the significantly enriched molecular function (MF) (Fig. 4D). The specific genes associated with the most significant pathways are shown in Fig. 4E.

3.3 Construction of the prognostic analysis model

We identified 15 DEGs between clusters C1 and C2 through Cox regression, and further performed LASSO regression to select the genes with prognostic significance. Seven genes, namely IL1B, CXCR4, CXCL10, SPP1, IFI27, ISG20 and FCGRT, were used to construct a prognostic model (Fig. 5A-B). The Risk score was calculated as below:
According to the median risk score, the patients were divided into the low-risk group and the high-risk group. As shown in Fig. 5C, CXCL10, IFI27 and ISG20 were significantly elevated in the low-risk group, while no significant difference was found in the expression levels of CXCR4, FCGRT, IL1B and SPP1 between the two groups. Furthermore, the high-risk groups showed worse prognosis in the training set (Fig. 5D-F), as well as in the external GSE53963 cohort consisting of 173 patients (Fig. 5G-I). Multivariate Cox analysis identified IL-1B as an independent risk factor for OC, and CXCR4 and ISG20 were identified as the protective factors (Fig. 6A). The chromosomal distribution of the 7 hub genes is shown in Fig. 6B. We integrated the clinical stages, age and disulfidptosis-based risk score into a predictive nomogram (Fig. 6C). The correlation between the expression levels of the 7 key genes is shown in Fig. 6D.

3.4 Relationship of disulfidptosis score with immune landscape and mutation profile of OC

The degree of immune infiltration was evaluated by calculating the enrichment score of the immune-related gene sets in the two risk groups using the ssGSEA algorithm. The immune infiltration landscape is shown in the boxplot in Fig. 7A. The abundance of the activated CD4 + and CD8 + T cells were higher in the low-risk group compared to that in the high-risk group. In contrast, the Tregs and myeloid-derived suppressor cells (MDSCs) were less abundant in the low-risk group, which likely contributed to an immunosuppressive microenvironment. However, we also observed a decrease of the abundance of immature, activated and plasmacytoid dendritic cells (DCs) in the low-risk group, which warrants further investigation. The abundance of activated CD4 + T cells was negatively correlated with the risk score, whereas that of Tregs, mast cells, neutrophils, NK cells, macrophages and monocytes were positively correlated with the risk score (Fig. 7B). The abundance of 67 immune cell subsets was further quantified using xcell algorithm on the basis of transcriptomic data. As shown in Fig. 8A, the abundance of iDCs, monocytes, CD8 + T cells, CD8 + Tcm cells, fibroblasts and pericytes were significantly different between the two risk groups. As shown in Fig. 8B, several infiltrating immune cell subsets were correlated with IL1B and CXCL10 expression. Finally, the mutation profile in TCGA-OV dataset was also analyzed, and the top 20 mutated genes in the high- and low-risk groups are shown in Fig. 8C.

3.5 IL1B is a potential oncogene in OC

We detected of the expression of IL-1B in six common ovarian cancer cell lines using Western blotting(Fig. 9A). To further determine the biological relevance of IL1B, we knocked down the gene in two OC cell lines (A780 and SKOV3) and validated the reduction in IL1B protein levels (Fig. 9B). IL1B knockdown significantly decreased the colony forming capacity (Fig. 9C-D) and the proliferation rates (Fig. 9E-F). The Transwell assay further showed that knocking down IL1B in the SKOV3 and A2780 cells led to a significant decrease in their migration and invasion ability (Fig. 9G-H). We also established an in vivo metastasis model of OV by intraperitoneally injecting luciferase-labeled control or IL1B-knockdown SKOV3 cells into BALB/c nude mice. We performed immunohistochemical experiments on tissue microarrays containing information on primary and metastatic foci from 48 ovarian cancer
patients. We found that IL1B expression was generally higher in the metastases than in the primary foci (Fig. 10A-B), and that patients with high IL1B expression had a relatively poor prognosis (Fig. 10C). As shown in Figure (10D-G), mice injected with the control cells showed stronger luciferase signal 18 days after inoculation, which indicated that IL1B silencing weakened the metastatic ability of the OC cells in vivo.

4 Discussion

Multiomics analysis of ovarian cancer and disulfidptosis

OC is a gynecological malignancy associated with high mortality rates [17]. It generally affects middle-aged and elderly women and is often asymptomatic in the early stage. OC patients with an insidious onset are often diagnosed at an advanced stage due to lack of early diagnostic markers, which increases the risk of metastasis and worsens prognosis [18]. The current standard of care for OC is a combination of surgery and chemotherapy, which has achieved limited efficacy. Therefore, it is crucial to identify novel biomarkers for early screening, improved prognosis prediction and effective therapeutic intervention in OC patients. Disulfidptosis is a newly discovered mechanism of programmed cell death, which may be a promising alternative target for cancer treatment. The aim of this study was to screen for disulfidptosis-related biomarkers in OC in order to identify potential prognostic indicators and therapeutic targets.

Summary of major findings

In this study, we analyzed the bulk RNA-seq data of 378 OC patients from TCGA-OV cohort, and the single-cell RNA-seq data of 4 high-grade SOC patients from GSE154600. Based on the disulfidptosis score, the individual cells in SOC patients were divided into subgroups that displayed distinct features, especially in cell communication. Seven prognostic genes were screened to construct a risk score-based predictive model, which was verified in an external cohort. The risk score was significantly associated with the immune landscape of OC. The oncogene IL1B had the highest risk coefficient and was further validated in cellular and animal models of OC. These findings provide novel insights into the molecular mechanisms of OC.

Biological functions of IL1B

Interleukin-1β (IL1B) is an inflammatory cytokine that plays a pivotal role in the host defense against injury and infection [19]. The pro-IL1B protein is primarily synthesized by activated macrophages, and is converted to its active form following proteolytic cleavage by caspase 1 (CASP1/ICE). As an inflammatory response mediator, IL1B is involved in a diverse range of cellular functions such as proliferation, differentiation, and apoptosis [20]. It is also a key player in the reproductive system [21], and regulates the ovulation process [22]. When administered ex vivo, IL1B effectively induces ovulation and synergizes with luteinizing hormone (LH) [23]. Furthermore, inactivation of the IL-1 receptor antagonist (IL-1RA) diminished LH-dependent ovulation [24]. IL1B and type I IL-1 receptor (IL-1R), along with other components of the intraovarian IL-1 system, are expressed during a brief periovulatory window [25]. In addition, IL1B prompts a multitude of ovulation-associated responses in rats, including stimulation of ovarian hyaluronic acid biosynthesis, perturbation of plasminogen activator and activation of nitric oxide (NO) synthase in the ovary, and cessation of follicular atresia [26]. IL1B is upregulated at the transcriptional level in the KGN cells by IL-15, which is markedly elevated in the follicular fluid of patients with polycystic ovary syndrome (PCOS) [27]. The production of IL1B by breast cancer cells is associated with bone metastasis in both clinical cohorts and pre-clinical in vivo models [28]. Furthermore, IL-1B is the master regulator of
breast tumor progression, and blocking IL1B can not only slow tumor growth but also facilitate checkpoint inhibition [29]. Taken together, IL1B has an important role in ovarian function and malignant transformation.

**IL-1B as a possible therapeutic target in OC**

Although IL1B is an established oncogene in many cancers [30–33], it has not been validated in OC so far. Our findings suggest that IL1B is an oncogene that promotes OC cell proliferation, migration and invasion. We will explore the role of IL1B in disulfidptosis in our subsequent study.

**Limitations and future work**

There are some limitations in this study that ought to be considered. First, the disulfidptosis-based model was constructed the basis of in-silico data, and needs to be validated further in animal models and clinical studies. The specific mechanisms underlying the function of these model genes also need further clarification. Although we identified IL1B as an oncogene, the role of free IL1B in the extracellular matrix was not discussed.

**5 Conclusion**

The disulfidptosis-based risk model can accurately predict the prognosis and immune characteristics of OC patients. The disulfidptosis-related gene IL1B functions as an oncogene, promotes proliferation, migration and invasion in OC and warrants further study as a potential therapeutic target.

**Declarations**

**Author Contribution**

**Conflict of Interest**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Ethics approval and consent to participate**

Mice were purchased from specific pathogen free (SPF) Vital River (Beijing, China). All animal experiments were performed under guidelines evaluated and approved by the Institutional Animal Care and Use Committee of the Chinese Academy of Medical Sciences Cancer Hospital.

The study was approved by the Ethics Committee of the National Cancer Center / Cancer Hospital, Chinese Academy of Medical Sciences, and Peking Union Medical College (Beijing, China).

**Consent for publication**

All authors of this article agree to the publication.

**Availability of data and materials**

All datasets involved in this study are included in the article or Additional files, and further inquiries can be directed to the corresponding author.
Competing interests
The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Authors’ contributions
KYW and BL made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

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References


Figures

Figure 1

Schematic illustration of the establishment of disulfidphtosis-related prognostic model and the experimental validation of IL1B in OV.
Figure 2

Characterization of cell types by disulfidptosis-related score. A. Umap of 6 cell populations after dimensionality reduction. B. Umap displaying the proportion of each cell type in the 4 OC patients. C. Umap showing disulfidptosis$^\text{high}$ and disulfidptosis$^\text{low}$ cells. D. Diagram showing high and low disulfidptosis gene set score in different cell groups. E. Proportion of different cell populations in the 4 OC patients. F. Dotplot showing specific marker genes for different cell populations.
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Figure 6

Figure 7

Construction of nomogram for predicting prognosis of OC patients. A. Forest plot of multivariate Cox analysis. B. Chromosomal distribution of 7 key genes. C. Illustration of the nomogram model. D. Correlation between the expression levels of the 7 key genes.
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The immune infiltration landscape in OC. A. Boxplot showing the infiltrating immune cells in the high-risk and low-risk groups based on ssGSEA algorithm. B. Scatter plots showing correlation between different immune cells and risk score.
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Functional verification of IL1B in ovarian cancer cells. A. Detection of the expression of IL-1B in six common ovarian cancer cell lines using Western blotting. B. Immunoblot showing efficiency of IL1B knockdown in SKOV3 and A2780 cell lines. C-D. Number of colonies formed by the control and IL1B-knockdown cells. E-F. Viability rates in the control and IL1B-knockdown groups. G-H. Results of Transwell assay.
Figure 11

Validation of the effects of IL1B, a key gene in a bisulfide death-related survival model, in clinical samples and in vivo experiments. A-B. IL1B expression in primary and metastatic foci of ovarian cancer patients. C. Survival curves of IL1B high expression and low expression groups. D-G. Abdominal metastasis model constructed after knocking down IL1B in ovarian cancer cells and effect analysis.