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SUGT1 is a prognostic biomarker and is associated with immune infiltrates in ovarian cancer

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Abstract

Background Ovarian cancer (OC) is a prevalent gynecological malignancy with a relatively dismal prognosis. The SGT1 homolog (SUGT1) protein, which interacts with heat shock protein 90 and is essential for the G1/S and G2/M transitions, was formerly thought to be a cancer promoter, but its precise role in OC remains unknown.

Methods We conducted a comprehensive bioinformatics analysis of SUGT1 expression in patients with OC compared with their normal controls, including the data from the cancer genome atlas (TCGA), genotype–tissue expression (GTEx) databases, gene ontology (GO) analysis, Kyoto Encylopedia of Genes and Genomes (KEGG) analysis, gene set enrichment analysis (GSEA), single sample gene set enrichment analysis (ssGSEA). In addition, Kaplan–Meier (KM) analysis, univariate and multivariate Cox analyses were applied to investigate the prognostic role of SUGT1 in ovarian cancer. Furthermore, we validated the expression of SUGT1 in OC and normal tissues through immunohistochemistry.

Results SUGT1 was significantly overexpressed in OC than in normal tissues. In addition, the GO, KEGG and GSEA analysis revealed that SUGT1 was associated with the functions related to immunoglobulin complex, antigen binding, immunoglobulin receptor binding, among others. Besides, ssGSEA demonstrated a positive correlation between SUGT1 expression and the abundance of T central memory cells, natural killer cells, and T gamma delta cells, although it showed a negative association with activated dendritic cells, cytotoxic cells, T cells, and T helper 1 cells. Subsequently, KM survival analysis revealed that high SUGT1 expression indicated a shorter overall survival, disease specific survival and progression free interval in OC patients. Univariate and multivariate Cox regression revealed that SUGT1 could serve as an independent risk factor for prognosis of patients with OC.

Conclusions All these results of this study show that SUGT1 is an important molecular component in immune infiltration in OC and may have a new significant prognostic role in OC.

Keywords Ovarian cancer, SUGT1, Prognosis, Immune infiltration, Biomarker

Introduction

Worldwide, ovarian cancer (OC) is the fifth most deadly type of cancer in women. It is a prevalent cancer of the female reproductive system [1]. Every year, over 300,000 women are infected by OC, and around 152,000 women die as a result of this disease. The incidence rate is 3.4%, with a 4.7% fatality rate [2]. This sobering statistic underscores the grave threat that ovarian cancer poses to women's health and survival.

†#These authors have contributed equally to this work and authors declare no conflicts of interest.

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The prognosis for patients with OC is notably bleak, with a less than 30% 5-year overall survival rate for advanced OC[3]. Conventional treatment regimens consist of platinum-based chemotherapy and cytoreductive surgery [4], with targeted therapies such as poly (ADP-ribose) polymerase inhibitors and antibodies against vascular endothelial growth factor reserved for specific cases [5]. Despite these efforts, more than half of the patients experience recurrence within 2 years, offering little improvement in survival rates [6, 7]. Research shows that early stage patients with OC had a 92% 5-year survival rate compared with 29% for late-stage cases [8]. The challenge in treating OC lies in its propensity to advance rapidly from an early to an advanced stage within a year, often without characteristic early symptoms, resulting in over 70% of patients receiving a diagnosis at an advanced stage [9, 10]. Despite recent advancements in treatment, progress in improving the 5-year survival rate has been slow [11]. Considering the limitations of current OC therapies, there is a pressing need for new therapeutic targets to enhance clinical outcomes. Consequently, reliable prognostic models are urgently required to facilitate the development of more targeted and effective treatments.

Heat shock protein 90 (Hsp90) cochaperones have sparked interest as candidate targets for cancer therapy, because they recruit clients to Hsp90 and regulate its activity [12]. As a cochaperone of Hsp90, SUGT1 is a highly conserved protein that is gaining increasing attention for its crucial function in cellular processes [13–15]. Several studies have linked SUGT1 to a variety of physiological processes, including cyclic AMP pathways, immunological responses, and ubiquitination [16–19]. Furthermore, its role alongside Hsp90 in kinetochore assembly, and kinetochore–microtubule attachment has been established [20, 21]. Notably, SGT1 and Hsp90 stabilize Scribbles to support hepatocyte growth factor-mediated epithelial morphogenesis and influence the positioning of Par and Pins complexes, which contributes to the establishment of neuroblast cortical polarity [22, 23].

SUGT1 overexpression has been reported in tumor tissues, most notably in colorectal cancer, where it is associated with increased recurrence rates and shorter survival [24]. Overexpression of SUGT1 in gastric carcinoma cells increases Akt phosphorylation by boosting the breakdown of the phosphatase PHLPP1, strengthening its association with SCF-β-TrCP [25]. Moreover, Ogi. H found that SUGT1 loss destabilizes the oncogenic fusion proteins PAX3-FOXO1 and EWS-FLI1, which are needed for cell development, reducing rhabdomyosarcoma and Ewing sarcoma proliferation [13]. The data indicate that the overexpression of SUGT1 contributes to the development of tumors.

Despite these known findings, the precise mechanisms and prognostic significance of SUGT1 in OC have been relatively overlooked. To determine the significance of elevated SUGT1 expression in OC, we conducted a comprehensive bioinformatics analysis of SUGT1 RNA expression data from patients with OC and corresponding clinical characteristics from the Cancer Genome Atlas (TCGA) datasets. Furthermore, we develop a predictive nomogram to predict the survival of patients with OC using clinicopathological variables and SUGT1 mRNA expression. Our results show SUGT1 have a pleiotropic role in the pathogenesis of OC and its overexpression was associated with a poor prognosis of OC, indicating that SUGT1 may be a novel prognostic biomarker in OC.

Materials and methods

Data collection and analyzing

The TCGA project provided the messenger RNA (mRNA) expression data for SUGT1 and the clinical information of patients with OC (https://portal.gdc.cancer.gov/) [26]. In addition, we used the genotype–tissue expression (GTEx) database to obtain mRNA expression data for SUGT1 from normal ovarian tissues. Transcripts per million reads were created from the Level 3 HTSeq-FPKM data for 427 patients with ovarian serous cystadenocarcinoma (OC) to facilitate further investigation. The 427 samples' clinical features that were either unknown or unattainable were considered missing data in those situations.

Expression analysis of SUGT1

We divided the samples into disease states (tumor or normal) and made scatter plots and boxplots to show the variations in SUGT1 expression to examine the differential expression of SUGT1 between OC and normal samples. SUGT1 expression levels were classified as SUGT1-Low or SUGT1-High based on statistical ranking, depending on whether they were below or above the median value.

Differentially expressed genes (DEGs) identification

Using the DESeq2 (4.0) program and the student's *t* test, a differential expression analysis between the SUGT1-High and SUGT1-Low expression OC groups was performed. Genes with a logarithm fold change (FC) > 1 and an adjusted $P < 0.05$ were deemed statistically significant. Volcano graphs were created to display all DEGs.

Analysis of gene–gene and protein–protein interactions

Protein–protein interactions (PPI) and gene–gene interaction networks involving SUGT1 were examined using STRING (https://cn.string-db.org) and GeneMANIA (http://www.genemania.org) [27, 28] GeneMANIA incorporates a variety of bioinformatic techniques, such as site prediction, co-localization, co-expression, physiological interaction genetic relationships, and gene enrichment analysis. Pairs with an interaction score > 0.90 were chosen for PPI.

Co-expression gene analysis of SUGT1 in OC

Using TCGA transcriptome sequence data, we identified the 30 leading positively and negatively related co-expression genes with SUGT1 in OC. For statistical analysis, the "Stat" package was utilized. For visualization, the "ggplot2" software was employed.

Functional enrichment analysis and tumor microenvironment exploration

DEGs were assessed for their biological effects by gene ontology (GO) and the Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses. In both investigations, statistical significance was determined using a count of 5 to 5000, a $P < 0.05$, and an FDR < 0.25. The SUGT1-High and SUGT1-Low groups' biological activities and pathways were assessed using Gene Set Enrichment Analysis (GSEA). Significant gene sets were defined as those having an absolute normalized enrichment score > 1, an adjusted $P < 0.05$, and an FDR < 0.25. The gene sets were provided using the Molecular Signature Database (MSigDB) (www.gsea-msigdb.org). Based on gene expression profiles, the infiltration levels of 24 distinct immune cell types were measured using the GSVA program and single-sample gene set enrichment analysis (ssGSEA) [29]. The relationship between immune cell infiltration levels and SUGT1 mRNA expression was assessed through Wilcoxon rank sum tests and Spearman correlation analysis.

Prognostic evaluation

To find out whether SUGT1 expression was associated with OC prognosis, we investigated disease-specific survival (DSS), overall survival (OS), and progression-free interval (PFI). The TCGA-OV dataset was subjected to univariate and multivariate Cox analyses to determine the predictive value of SUGT1 mRNA expression. The median level of OC mRNA expression was used to derive the cutoff value. The predictive value was subsequently assessed independently using SUGT1 mRNA levels, followed by the application of multivariate Cox analysis.

Nomogram construction

We created nomograms utilizing the "rms" and "survival" programs for analysis and visualization to anticipate the 1-, 3-, and 5-year OS for OC patients. The accuracy of the nomogram's probability predictions concerning the actual occurrences was graphically assessed using calibration curves.

Immunohistochemistry (IHC)

Immunohistochemistry studies on ovarian tissues were performed according to the manufacturer's instructions (using antibody 11675-1-AP, China, Proteintech). Rehydration, deparaffinization, antigen retrieval, quenching endogenous peroxidase activity, and blocking were involved. After that, the tissues were subjected to overnight incubation at 4 °C with the primary antibody (diluted 1:400) and for 30 min at 37 °C with the horseradish peroxidase-tagged secondary antibody. The SUGT1 expression was evaluated through the H-SCORE method, calculated as follows: (1 × percentage of weak staining) + (2 × percentage of moderate staining) + (3 × percentage of strong staining) within the target region, ranging from 0 to 300 [30].

Statistical analysis

All statistical analyses were performed using R (v4.2.1) and RStudio software. In the initial data analysis, two-tailed Student's t tests and one-way analysis of variance (ANOVA) were performed. To evaluate statistical significance, a $P < 0.05$ was used.

Results

SUGT1 mRNA expression in human cancers

We started by comparing SUGT1 mRNA expression in human cancer tissues to normal tissues using TCGA and GTEx data. We found that 27 out of the 33 cancer types under investigation had significantly different levels of SUGT1 expression, 24 of which had considerably higher levels of SUGT1 expression and three of which had significantly lower levels. This extensive analysis of SUGT1 in a variety of cancer tissues suggests that it may serve as a tumor promoter. Specifically, SUGT1 was significantly overexpressed in breast invasive carcinoma, cervical squamous cell carcinoma, esophageal carcinoma, bladder urothelial carcinoma, endocervical adenocarcinoma, rectum adenocarcinoma, kidney renal clear cell carcinoma, head and neck squamous cell carcinoma, colon adenocarcinoma, lymphoid neoplasm diffuse large B-cell lymphoma, lung squamous cell carcinoma, cholangiocarcinoma, glioblastoma multiforme, pancreatic adenocarcinoma, liver hepatocellular carcinoma, prostate adenocarcinoma, lung adenocarcinoma, OC, skin cutaneous melanoma, uterine corpus endometrial

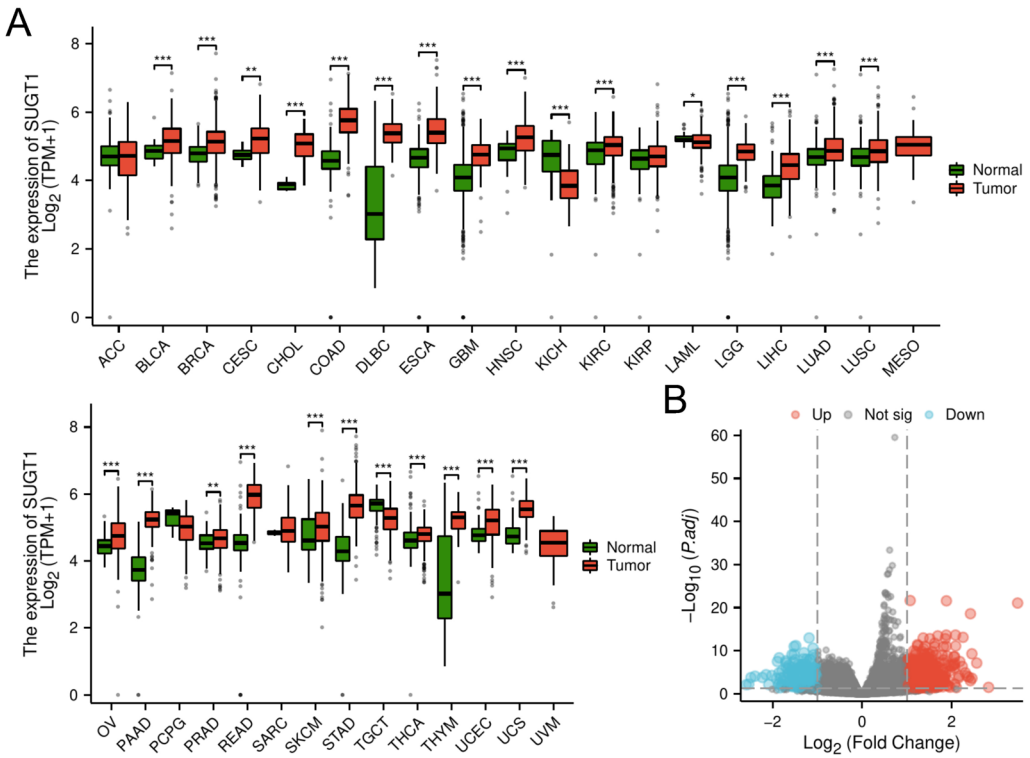

Fig. 1 Pan-cancer levels of SUGT1 mRNA. **A** Expression of SUGT1 in TCGA and GTEx databases' normal (unpaired) and cancerous samples. **B** Volcano graphic of the genes with differential expression. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. GTEx: the Genotype–Tissue Expression; TCGA: the Cancer Genome Atlas

carcinoma, stomach adenocarcinoma, uterine carcinosarcoma, thymoma, and thyroid carcinoma. In contrast, lower expression of SUGT1 mRNA existed in testicular germ cell tumors, acute myeloid leukemia, and kidney chromophobe ($P < 0.05$) (Fig. 1A).

Identification and analysis of DEGs in OC

To examine the variations in gene expression between 190 SUGT1-Low and 191 SUGT1-High samples in OC, 849 DEGs were identified. A total of 650 of these were found to be upregulated, whereas 199 were downregulated. The volcano diagram that visually represents these DEGs is displayed in Fig. 1B. The STRING database and GeneMANIA were used to create protein–protein and gene–gene interaction networks to identify SUGT1-related target proteins and genes (Fig S1).

Functional enrichment and mechanism exploration in OC

To understand more about the biological functions and mechanisms behind SUGT1 in OC, we performed GO and KEGG enrichment analyses on DEGs associated with the protein. The function of these DEGs in various biological processes, cellular components, and molecular functions is illustrated in Fig. 2A. Among these processes were neuroactive ligand–receptor interaction, immunoglobulin complex, phagocytosis, and antigen binding. The GSEA was performed by comparing samples with high and low SUGT1 expression to further elucidate the SUGT1-associated pathway. Notably, the SUGT1-high expression phenotype was significantly associated with hedgehog signaling, epithelial–mesenchymal transition (EMT), and KRAS signaling DN (Fig. 2B–D). On the other hand, the SUGT1-low expression phenotype was significantly associated with inflammatory response, adipogenesis, TNFα/NF-κB, oxidative phosphorylation, TAK JAK STAT3 signaling, apoptosis, mtorc1 signaling, and fatty acid metabolism (Fig. 2E–L). These results provide insight into the possible functions of SUGT1 in OC as well as its effects on pertinent pathways and processes.

Correlation with immune infiltration

Using ssGSEA, we employed Spearman correlation to demonstrate the relationship between SUGT1 expression and immune cell infiltration levels in the setting of an OC tumor(Fig.3A). Figure 3B–D ($P < 0.05$) demonstrates a substantial negative correlation between SUGT1 expression and the number of activated dendritic cells (aDC) ([$R = -0.301$, $P < 0.001$], Fig. 3B),

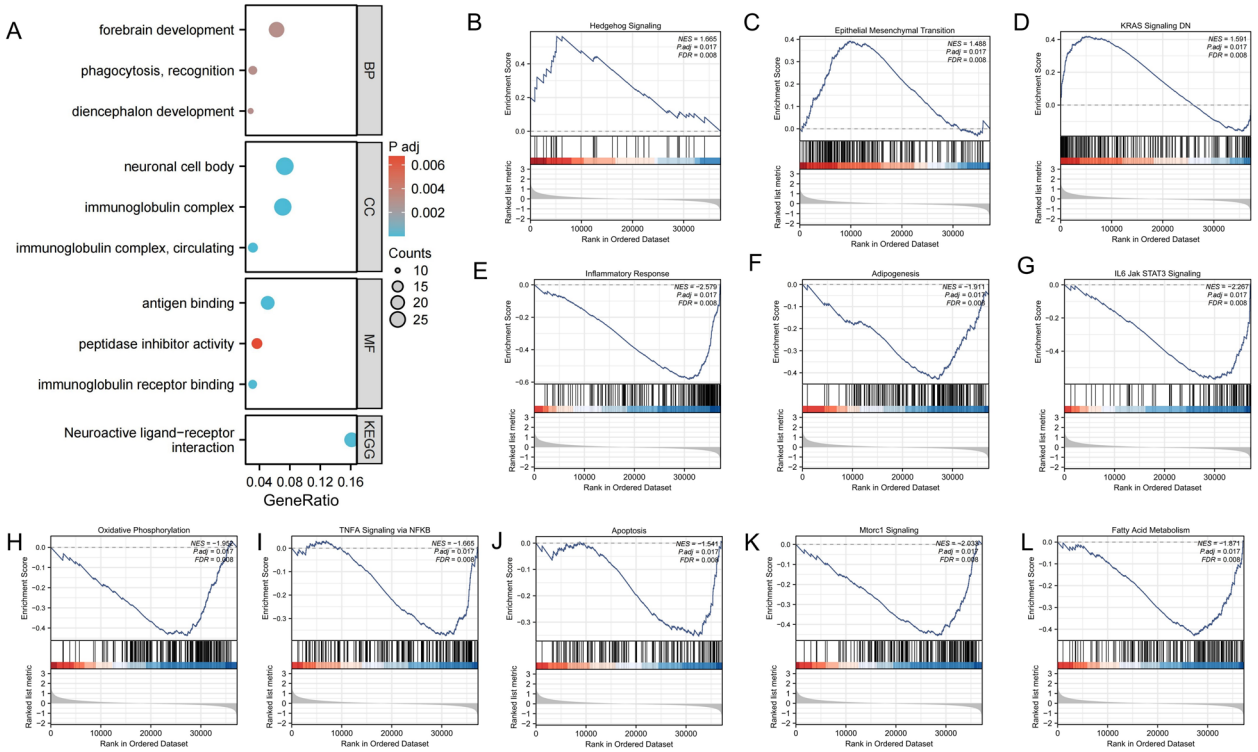

Fig. 2 Functional enrichment analysis of SUGT1 in OC. **A** GO and KEGG enrichment analyses of DEGs in OC. **B**–**L** GSEA revealed SUGT1-related signaling pathways in h.all.v2022.1.Hs.symbols.gmt. **B** Hedgehog signaling pathway; **C** epithelial–mesenchymal transition pathway; **D** KRAS signaling DN pathway; **E** inflammatory response; **F** adipogenesis; **G** IL6 JAK STAT3 signaling; **H** oxidative phosphorylation; **I** TNFA signaling via NF-κB; **J** apoptosis; **K** Mtorc1 signaling; **L** fatty acid metabolism

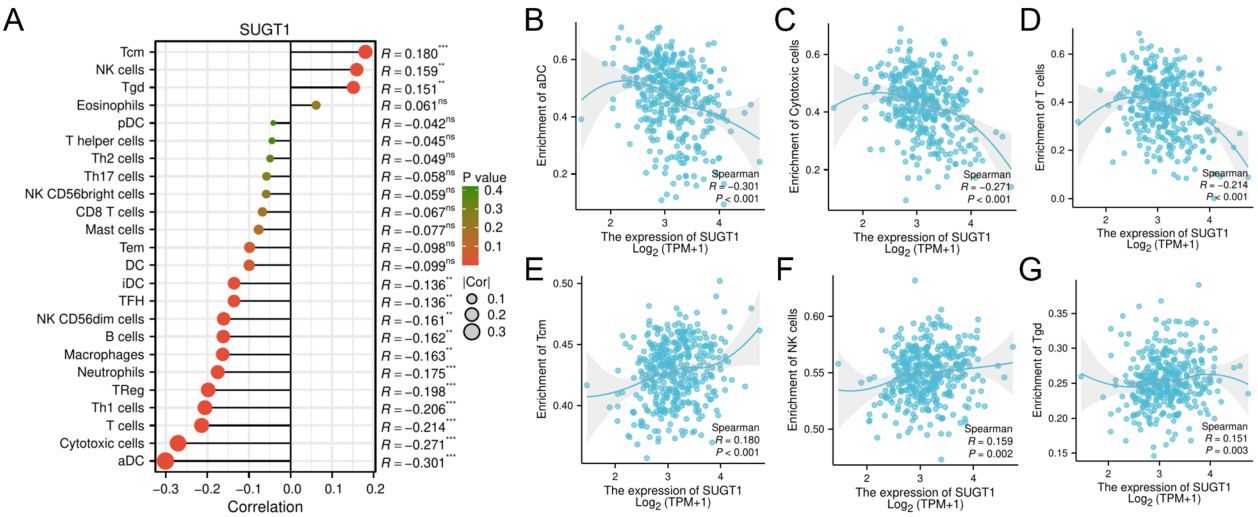

Fig. 3 Relationship between SUGT1 expression in the tumor microenvironment of OC and immune cell infiltration. **A** Relationship between immune cell levels and SUGT1 mRNA expression. The relationships between the abundances of (**B**) aDC, (**C**) cytotoxic cells, (**D**) T cells, (**E**) Tcm, (**F**) NK cells, and (**G**) Tgd cells are shown in scatter plots (**B**–**G**). Tcm, or central memory T cells; aDC, or activated dendritic cells

cytotoxic cells ([$R=-0.271$, $P<0.001$], Fig.3C), T cells ([$R=-0.214$, $P<0.001$], Fig.3D), and SUGT1 expression are positively with T central memory (Tcm) cells ([$R=0.180$, $P<0.001$], Fig.3E), natural killer (NK) cells ([$R=0.159$, $P<0.001$], Fig.3F) and T gamma delta (Tgd) cells ($R=0.151$, $P<0.001$) (Fig. 3G).

Co-expression gene analysis

The heatmaps showed the top 30 genes that correlated either positively or negatively with SUGT1 expression in OC. SUGT1 was most positively correlated with *GTF2F2*, *NUFIP1*, *TRIM13*, *MED4*, and *GPALPP1*, as Figure S2A illustrates. The most negatively linked variables with SUGT1 in OC were *UBE2L6*, *NUDT8*, *PLAAT4*, *LGALS17A*, and *PIGR*, according to the heatmap of negative relationships (Fig S2B).

Association with clinicopathological variables

We obtained gene expression and clinical information for 381 OC patients from the TCGA database. These patients were divided into groups with high or low SUGT1 expression based on the mean SUGT1 expression value (Table 1), and any potential correlations between SUGT1 expression and clinical characteristics were evaluated. Logistic regression analysis revealed no significant correlation between SUGT1 mRNA expression and clinical factors, such as tumor-node-metastasis stage, age, race, main therapeutic result, histologic grade, anatomic neoplasm subdivision, venous invasion, and lymphatic invasion ($P > 0.05$, Table 2).

Table 1 Relationship between SUGT1 mRNA expression and clinical characteristics in OC

Characteristics	Low expression of SUGT1	High expression of SUGT1	*P* value
n	190	191	
Clinical stage, *n* (%)			0.185
Stage I	0 (0%)	1 (0.3%)	
Stage II	14 (3.7%)	9 (2.4%)	
Stage III	141 (37.3%)	155 (41%)	
Stage IV	34 (9%)	24 (6.3%)	
Race, *n* (%)			0.528
Asian	7 (1.9%)	5 (1.4%)	
White	164 (44.7%)	166 (45.2%)	
Black or African American	10 (2.7%)	15 (4.1%)	
Tumor status, *n* (%)			0.986
Tumor free	35 (10.4%)	37 (10.9%)	
With tumor	129 (38.2%)	137 (40.5%)	
Primary therapy outcome, *n* (%)			0.112
PD	8 (2.6%)	19 (6.1%)	
SD	10 (3.2%)	12 (3.9%)	
PR	21 (6.8%)	22 (7.1%)	
CR	117 (37.9%)	100 (32.4%)	
Age, *n* (%)			0.163
≤ 60	111 (29.1%)	98 (25.7%)	
> 60	79 (20.7%)	93 (24.4%)	
Histologic grade, *n* (%)			0.738
G1 & G2	22 (5.9%)	24 (6.5%)	
G3 & G4	164 (44.2%)	161 (43.4%)	
Anatomic neoplasm subdivision, *n* (%)			0.252
Bilateral	138 (38.4%)	119 (33.1%)	
Left	24 (6.7%)	32 (8.9%)	
Right	21 (5.8%)	25 (7%)	
Venous invasion, *n* (%)			0.525
No	16 (15.2%)	25 (23.8%)	
Yes	29 (27.6%)	35 (33.3%)	
Lymphatic invasion, *n* (%)			0.750
No	21 (14.1%)	27 (18.1%)	
Yes	47 (31.5%)	54 (36.2%)	

Table 2 SUGT1 mRNA expression association with clinical pathological characteristics (logistic regression)

Characteristics	Total (*N*)	OR (95% CI)	*P* value
Clinical stage (Stage III & Stage IV vs. Stage I & Stage II)	378	1.432 (0.620–3.310)	0.401
Tumor status (With tumor vs. Tumor free)	338	1.005 (0.597–1.691)	0.986
Primary therapy outcome (CR vs. PD & SD & PR)	309	0.629 (0.384–1.029)	0.065
Age (> 60 vs. ≤ 60)	381	1.333 (0.890–1.998)	0.163
Histologic grade (G3 & G4 vs. G1 & G2)	371	0.900 (0.485–1.670)	0.738
Venous invasion (Yes vs. No)	105	0.772 (0.348–1.715)	0.526
Lymphatic invasion (Yes vs. No)	149	0.894 (0.448–1.784)	0.750

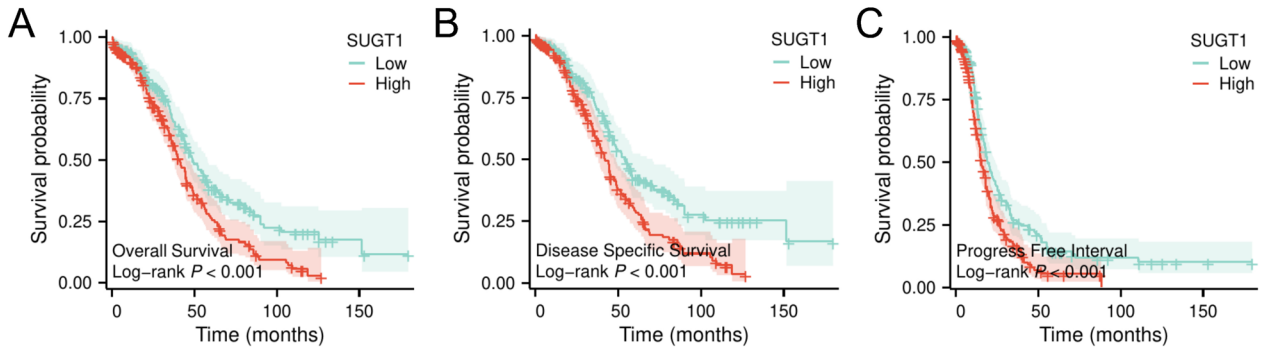

Fig. 4 SUGT1-high and SUGT1-low groups in OC were compared using Kaplan–Meier survival plots with the TCGA database. The analysis included three measures: **A** overall survival, **B** disease-specific survival, and **C** progression-free interval

Prognostic value of SUGT1 in OC

High SUGT1 expression was linked to poor OS, DSS, and PFI, according to survival analysis (Fig. 4A–C). Patients with OC and high SUGT1 expression exhibited poor OS (hazard ratio [HR] = 1.551 [1.195–2.011], $P < 0.001$) (Table 3), poor DSS (HR = 1.651 [1.245–2.189], $P < 0.001$) (Table S1), and poor PFI (HR = 1.512 [1.189–1.921], $P < 0.001$) (Table S2), according to univariate Cox regression analysis. A multivariate Cox regression analysis showed that poor OS (HR = 1.406 [1.040–1.900], $P = 0.027$) (Table 3), DSS (HR = 1.372 [1.011–1.861], $P = 0.042$) (Table S1), and PFI (HR = 1.611 [1.234–2.103], $P < 0.001$) (Table S2) were independently associated with increased expression of SUGT1.

The development and testing of an SUGT1-related nomogram

We developed a nomogram to predict OC patients' prognoses on the basis of SUGT1 expression and other independent clinical variables. The nomogram was utilized to predict 1-, 3- and 5-year OS, DSS and PFI in OC (Figs. 5A, S3A and S4A). Furthermore, the calibration curve was constructed to evaluate the efficiency of the nomogram (Figs. 5B, S3B and S4B). The 1-, 3- and 5-year OS, DSS and PFI lines was close to ideal line, indicating that the nomogram model demonstrated satisfactory accuracy.

SUGT1 is overexpressed in patients with OC

To validate the consistency of SUGT1 expression in OC tissues, IHC was conducted, comparing SUGT1 expression between patients with OC ($n = 17$) and their normal controls ($n = 18$). The findings showed that OC had higher SUGT1 expression than the control samples, suggesting that SUGT1 may play a crucial role in OC (Fig. 6A, B).

Discussion

A highly conserved protein called SUGT1 functions as a Hsp90 cochaperone [13–15]. Previous studies have documented upregulated SUGT1 expression in xenografts and cancer tissues [13, 24, 25]. SUGT1 is involved in several distinct physiological processes, including immune response [18, 19], cyclic AMP pathway [17], and ubiquitination [16, 17]. These outcomes raised the possibility that SUGT1 is an oncogene. However, little is known about SUGT1's underlying mechanism or prognostic significance in ovarian cancer.

Despite multiple studies, the prognosis for OC remains dismal, with a less than 30% 5-year overall survival rate for advanced OC [3]. As a result, it is critical to

Table 3 Univariate and multivariate analyses (overall survival) for prognostic factors in ovarian cancer

Characteristics	Total (*N*)	Univariate analysis		Multivariate analysis	
		Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
Clinical stage	376				
Stage I & Stage II	24	Reference		Reference	
Stage III & Stage IV	352	2.135 (0.947–4.811)	0.067	1.548 (0.571–4.200)	0.391
Age	379				
≤ 60	207	Reference		Reference	
> 60	172	1.352 (1.045–1.749)	0.022	1.388 (1.028–1.875)	0.033
Histologic grade	369				
G1 & G2	46	Reference			
G3 & G4	323	1.239 (0.838–1.833)	0.283		
Lymphatic invasion	148				
No	48	Reference			
Yes	100	1.413 (0.833–2.396)	0.200		
Primary therapy outcome	308				
PD & SD & PR	91	Reference		Reference	
CR	217	0.232 (0.168–0.322)	< 0.001	0.298 (0.213–0.417)	< 0.001
Venous invasion	105				
No	41	Reference			
Yes	64	0.896 (0.487–1.649)	0.723		
Tumor status	337				
Tumor free	72	Reference		Reference	
With tumor	265	9.598 (4.487–20.532)	< 0.001	9.208 (3.730–22.731)	< 0.001
SUGT1	379				
Low	189	Reference		Reference	
High	190	1.551 (1.195–2.011)	< 0.001	1.406 (1.040–1.900)	0.027

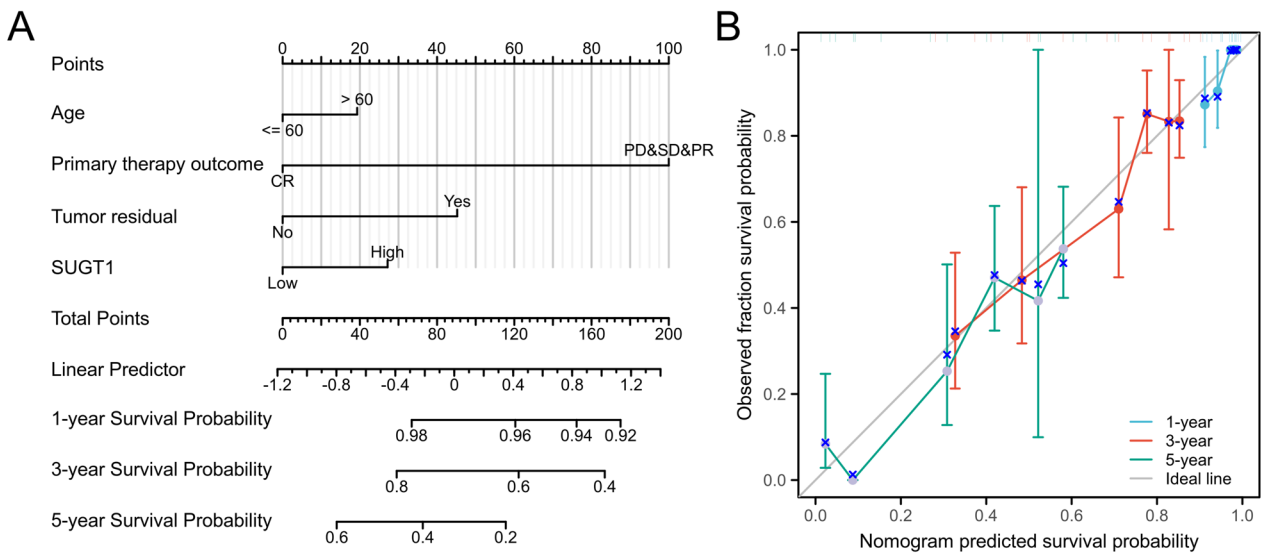

Fig. 5 Ovarian cancer prognostic model that predicts 1-, 3-, and 5-year overall survival (OS). **A** Nomogram for predicting the chance of an OC patient's OS of 1, 3, and 5 years. **B** Nomogram calibration plots are used to calculate the risk of OS after 1, 3, and 5 years

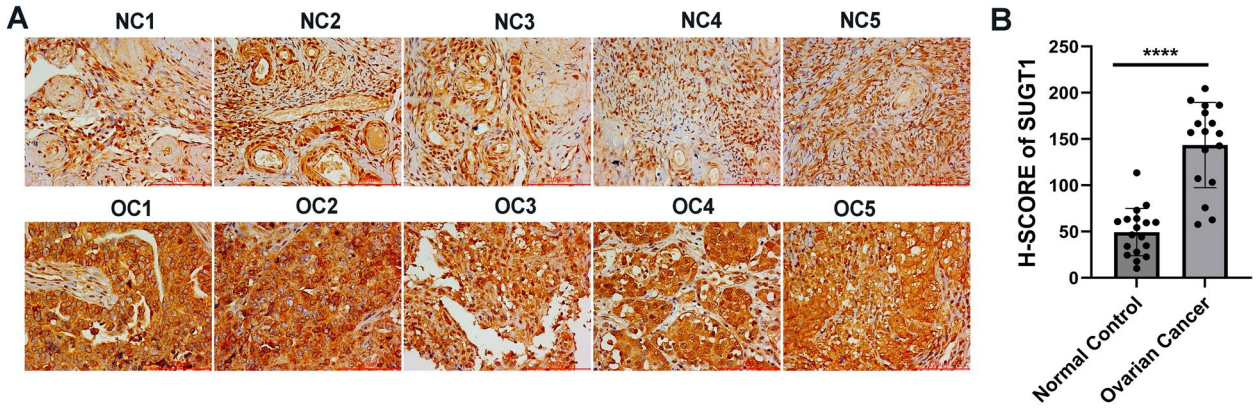

Fig. 6 High SUGT1 expression was observed in patients with OC. **A** Representative immunohistochemistry images of SUGT1 expression in the ovarian tissues of patients with and without OC. **B** The staining intensity of SUGT1 expression was assessed using H-SCORE analysis ($n = 17$ in the OC group, $n = 18$ in the normal control group)

identify effective and persuasive prognostic and therapeutic targets for OC patients. Based on this, in the current work, we use IHC and publicly available datasets to examine the expression and prognostic significance of SUGT1 mRNA expression in OC.

According to the current study, SUGT1's mRNA expression was significantly higher in 24 types of cancer than in normal tissues, suggesting that it may have an oncogene role in human cancers. To gain a deeper understanding of the biological activities and processes of SUGT1 in OC, GSEA, GO, and KEGG analyses were employed. The findings of KEGG enrichment and GO analyses demonstrated the involvement of the DEGs in phagocytosis, recognition, immunoglobulin complex, antigen binding, immunoglobulin receptor binding, and neuroactive ligand–receptor interaction. Recent research has shown that phagocytosis is essential to tumor formation and offers prospective targets for anti-cancer medications [31, 32]. Future investigations on the function of SUGT1 in OC were sparked by these findings. According to GSEA results, SUGT1 was linked to pathways related to "hedgehog signaling," "epithelial-mesenchymal transition (EMT)," "KRAS signaling," "inflammatory response," "adipogenesis," "IL6 JAK STAT3 signaling," "oxidative phosphorylation," "TNFα/NF-Kb," "apoptosis," "mtorc1 signaling," and "fatty acid metabolism." These pathways have been linked to the invasion, metastasis, and proliferation of cells in OC [33–35].

Tumor immune infiltration cells (TIIC) paly a double-edged role in the development of OC, which can help cancer cells evade immune surveillance but also limit the growth of tumors [36]. The ssGSEA method was used to assess the correlation between SUGT1 mRNA expression and the abundance of TIICs in OC. The results showed that the numbers of Tcm cells, NK cells, and Tgd cells were significantly associated with SUGT1 mRNA expression, whereas the numbers of aDC cells, cytotoxic cells, and T cells were not. DCs are crucial antigen-presenting cells, and aDCs are required for the start of an effective T cell response and the recruitment of T cells to tumor tissues for cancer cell-killing impact [37, 38]. These findings help to explain why SUGT1 mRNA expression exhibits a negative correlation with OC patient survival. However, it should be noted that the link between TIICs and SUGT1 mRNA expression was based solely on TCGA database analysis results, and the TIIC correlation coefficient was not high. The complicated interactions between TIICs and the OC tumor immune microenvironment need to be validated and explored further.

This study aimed to evaluate the correlation between SUGT1 mRNA expression and the prognosis for patients with OC. Longer OS, DSS, and PFI durations were found to be substantially linked to decreased SUGT1 mRNA expression in a Kaplan–Meier survival assessment. The expression of SUGT1 mRNA was found to be an independent and reliable predictive indicator for patients with OC in both univariate and multivariate Cox regression analyses. Furthermore, we developed a predictive nomogram that uses clinicopathological variables and SUGT1 mRNA expression to forecast the survival of patients with OC.

Despite the comprehensive analysis regarding the link between OC and SUGT1 mRNA expression, our investigation had several drawbacks. Larger clinical sample sizes are required to confirm the association between OC patient prognosis and SUGT1 expression. Second, there may be some bias, since confounding variables could have affected the results of the IHC study, whereby we received most of the raw data from public databases.

Furthermore, more research is needed to fully understand the molecular and functional pathways connected to SUGT1. Also, more research on the clinical relevance of SUGT1 in OC is necessary soon.

Conclusion

To the best of our knowledge, this investigation was the first to evaluate SUGT1's immunological and prognostic effects in OC. Notwithstanding, it is imperative to recognize the previously noted constraints, and a more comprehensive mechanistic investigation of SUGT1 is required. Overall, our research showed that high levels of SUGT1 mRNA represent a separate risk factor for OC patients and that SUGT1 expression is higher in OC tissues. Furthermore, the expression of this gene can be linked to immune cell infiltration within malignancies. In light of these findings, we suggest that SUGT1 might serve as a biomarker for OC prognosis.

Abbreviations

OC	Ovarian cancer
SUGT1	SGT1 homolog
TCGA	The cancer genome atlas
GTEx	Genotype–tissue expression
GO	Gene ontology
KEGG	Kyoto Encylopedia of Genes and Genomes
GSEA	Gene set enrichment analysis
ssGSEA	Single sample gene set enrichment analysis
KM	Kaplan–Meier
Hsp90	Heat shock protein 90
PPI	Protein–protein interactions
DEGs	Differentially expressed genes
MSigDB	Molecular signature database
OS	Overall survival
PFI	Progression-free interval
DSS	Disease-specific survival
IHC	Immunohistochemistry
ANOVA	One-way analysis of variance
H-SCORE	Histochemistry score
EMT	Epithelial–mesenchymal transition
TIIC	Tumor immune infiltration cells

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40001-024-02232-5.

Supplementary Material 1: Figure S1: Developing the interaction network for SUGT1.The STRING database is used to view the PPI network of SUGT1. The GENEMANIA database's SUGT1 gene-gene interaction network. PPI, protein-protein interaction.

Supplementary Material 2: Figure S2: SUGT1 co-expression analysis in Oncogene. The heatmap shows the top 30 OC genes strongly linked to SUGT1.There is a heatmap showing the top 30 OC genes that have SUGT1 negative correlates.

Supplementary Material 3: Figure S3: Ovarian cancer prognostic model that predicts 1-, 3-, and 5-year disease-specific survival.A nomogram for predicting the chance of an OC patient's DSS of 1, 3, and 5 years.Nomogram calibration plots are used to calculate the risk of DSS after one, three, and five years.

Supplementary Material 4: Figure S4: Ovarian cancer prognostic model that predicts 1-, 3-, and 5-year progression-free interval.A nomogram for predicting the chance of an OC patient's PFI of 1, 3, and 5 years.Nomogram calibration plots are used to calculate the risk of PFI after one, three, and five years.

Supplementary Material 5:Table S1: Univariate and multivariate analysis (disease specific survival) for prognostic factors in ovarian cancer.

Supplementary Material 6:Table S2: Univariate and multivariate analysis (progression free survival) for prognostic factors in ovarian cancer.

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Author contributions

Guanghui Song supervised the experiments and revised the article, Linyan Ge and Xiu Liu performed the experiments and analyzed the data , Linyan Ge wrote the manuscript, Lingyan Zhang and JiaRen Zhang collected the clinical samples.

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Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Sir Run Run Shaw Hospital, Zhejiang University School of Medicine. The ethical approval number is 2023-882-01. All samples were collected after participants signed written informed consent.

Consent for publication

The patient was informed that data concerning the case would be submitted for publication, and he consented.

Competing interests

The authors declare no competing interests.

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