Vol. 8, Issue 2, August 2026, pp 518-532
https://doi.org/10.36590/jika.v8i2.1604
http://salnesia.id/index.php/jika
jika@salnesia. id, p-ISSN: 2337-9847, e-ISSN: 2686-2883
Penerbit: Sarana Ilmu Indonesia (salnesia)

RESEARCH ARTICLES

Downregulation of RGS2 Expression in Ovarian Cancer: A TCGA–GTEx Transcriptomic Analysis

Penurunan Ekspresi RGS2 pada Kanker Ovarium: Analisis Transkriptomik Berbasis Data TCGA dan GTEx

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Abstract

Regulator of G protein signaling 2 (RGS2), a negative regulator of G protein-coupled receptor signaling, is implicated in ovarian cancer. Given the disease's late-stage diagnosis and poor prognosis, identifying reliable molecular biomarkers is crucial. This study evaluated RGS2 gene expression in ovarian cancer and its clinicopathological and prognostic associations using public transcriptomic data. RNA-sequencing data from 419 The Cancer Genome Atlas (TCGA) tumor samples and 88 Genotype-Tissue Expression (GTEx) normal samples were compared using the Mann-Whitney U test. Additionally, 308 TCGA cases were analyzed for associations with tumor grade, clinical stage, and survival outcomes—including overall survival (OS), disease-specific survival (DSS), progression-free interval (PFI), and disease-free interval (DFI) using the Kaplan-Meier method and log-rank tests based on median RGS2 expression. Results demonstrated that RGS2 was significantly down-regulated in ovarian cancer tissues compared to normal tissues ($p<0,001$). However, RGS2 expression showed no significant correlation with tumor grade, clinical stage, or any evaluated survival metrics (all $p>0,05$). In conclusion, while RGS2 is consistently down-regulated at the transcript level in ovarian cancer, it is not significantly associated with patient survival. These findings suggest that although reduced RGS2 expression is a common molecular feature of ovarian cancer, its utility as a standalone prognostic biomarker is limited in unstratified transcriptomic analyses.

Keywords: gene expression, ovarian cancer, rgs2, tcga, transcriptomic

Article history:

Submitted 16 August 2025
Accepted 05 July 2026
Published 04 August 2026

PUBLISHED BY:
Sarana Ilmu Indonesia (salnesia)
Address:
Jl. Dr. Ratulangi No. 75A, Baju Bodoa, Maros Baru, Kab. Maros, Provinsi Sulawesi Selatan, Indonesia

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Abstrak

Regulator pensinyalan protein G 2 (RGS2), sebuah regulator negatif pada pensinyalan reseptor berpasangan protein G, telah dikaitkan dengan kanker ovarium. Mengingat penyakit ini sering didiagnosis pada stadium lanjut dan memiliki prognosis yang buruk, identifikasi biomarker molekuler yang andal sangatlah penting. Penelitian ini mengevaluasi ekspresi gen RGS2 pada kanker ovarium serta hubungannya dengan karakteristik klinikopatologis dan prognosis menggunakan data transkriptomik publik. Data sekuensing RNA dari 419 sampel tumor The Cancer Genome Atlas (TCGA) dan 88 sampel normal Genotype-Tissue Expression (GTEx) dibandingkan menggunakan uji Mann-Whitney U. Selain itu, 308 kasus TCGA dianalisis untuk melihat kaitannya dengan derajat tumor, stadium klinis, dan hasil kesintasan termasuk kesintasan keseluruhan (overall survival/OS), kesintasan spesifik penyakit (disease-specific survival/DSS), interval bebas progresi (progression-free interval/PFI), dan interval bebas penyakit (disease-free interval/DFI) menggunakan metode Kaplan-Meier dan uji log-rank berdasarkan nilai median ekspresi RGS2. Hasil penelitian menunjukkan bahwa RGS2 mengalami penurunan regulasi (downregulated) secara signifikan pada jaringan kanker ovarium dibandingkan dengan jaringan normal (p<0,001). Namun, ekspresi RGS2 tidak menunjukkan korelasi yang signifikan dengan derajat tumor, stadium klinis, maupun metrik kesintasan mana pun yang dievaluasi (semua p>0,05). Kesimpulannya, meskipun RGS2 secara konsisten mengalami penurunan regulasi pada tingkat transkrip dalam kanker ovarium, ekspresinya tidak terkait secara signifikan dengan kesintasan pasien. Temuan ini menunjukkan bahwa meskipun penurunan ekspresi RGS2 merupakan ciri molekuler umum dari kanker ovarium, kegunaannya sebagai biomarker prognostik mandiri sangat terbatas dalam analisis transkriptomik yang tidak terstratifikasi.

Kata Kunci: *ekspresi gen, kanker ovarium, rgs2, tgca, transkriptomik*

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Highlight:

- *RGS2* gene expression is consistently downregulated in ovarian cancer tissue compared to normal ovarian tissue.
- The decreased expression of *RGS2* shows no significant correlation with either the clinical stage of the disease or the tumor grade.
- *RGS2* gene expression is not significantly associated with overall patient survival, indicating that it is inadequate for use as an independent prognostic biomarker.

INTRODUCTION

Ovarian cancer is one of the most prevalent malignancies of the female reproductive system and ranks as the leading cause of death among gynecologic cancers. It is frequently diagnosed at advanced stages, contributing to its poor prognosis and high mortality. According to the American Cancer Society (2023), there were an estimated 19,710 new cases and 13,270 deaths from ovarian cancer in the United States, placing it fifth among cancer-related deaths in women. The average age at diagnosis is 63 years, with a five-year relative survival rate of only 50.8% (Surveillance Research Program, 2026). In Indonesia, ovarian cancer ranks third among the most common

cancers in women, with 14,896 new cases and 9,581 deaths reported in (Ferlay *et al*., 2021).

Cancer cells grow uncontrollably, avoid apoptosis, and can spread to other tissues and organs through metastasis. Changes in intracellular signaling pathways are what cause these processes to happen. Mutations in signaling molecules are often what cause oncogenic transformation (Hanahan, 2022). The G protein-coupled receptor (GPCR) pathway is one of the most important mechanisms that leads to cancer. It sends signals from outside the cell through heterotrimeric G proteins (Lappano dan Maggiolini, 2023; Cheng L *et al*., 2023). Regulators of G Protein Signaling (RGS) are a very important group of proteins that control this pathway. They speed up the GTP hydrolysis of the Gα subunit, which stops signal transmission and changes the activity of GPCRs (Li L *et al*., 2023). RGS2, a member of this protein family, has gotten a lot of interest since it might help stop tumors from growing and is linked to a number of malignancies, such as breast, prostate, leukemia, lymphoma, bladder, and ovarian cancer.

RGS2 is encoded on chromosome 1 and consists of five exons. It is part of a group of RGS proteins that have short N-terminal extensions and RGS-box domains. RGS2 is a GTPase-activating protein (GAP) that controls Gαq signaling in a specific way. It also has other roles that don't depend on its GAP activity (Xu *et al*., 2023). Researchers have shown that green fluorescent protein (GFP)-tagged RGS2 is found in the nucleus, cytoplasm, and plasma membrane of human embryonic kidney (HEK293) cells (Heximer *et al*., 2001). RGS2 and other proteins like RGS16 may stop the activation of the epidermal growth factor receptor (EGFR), which means that there may be communication between signaling pathways that could be important for cancer progression (Yang *et al*., 2023).

Recent evidence suggests that RGS2 expression is frequently downregulated in ovarian and prostate cancers, which may contribute to enhanced cell proliferation and chemoresistance (Cacan, 2017). Epigenetic mechanisms, such as DNA methylation and histone deacetylation, have been implicated in the suppression of RGS2 and related genes like RGS10, which play a role in tumorigenesis and resistance to chemotherapeutic agents like cisplatin (Cacan, 2017; Lumpp *et al*., 2024). DNA methyltransferases (DNMTs) and histone deacetylases (HDACs) are among the key regulators in this silencing process, and their activity may account for the loss of RGS2 expression observed in resistant ovarian cancer cells (Lumpp *et al*., 2024; Cacan, 2017).

Although various advancements have been made, prognostic indicators for ovarian cancer are still limited to conventional clinical parameters such as FIGO stage, tumor histology, ascites cytology, and residual tumor size. Given the molecular heterogeneity of ovarian cancer, there is an urgent need to identify reliable predictive biomarkers that reflect tumor biology and therapy response (Hu *et al*., 2021). Ovarian cancer comprises multiple histopathological subtypes with distinct molecular and clinical features, which may influence the biological and clinical interpretation of individual gene expression profiles.

Recent data report that low expression of RGS2 is associated with poor prognosis in high-grade serous ovarian cancer, suggesting a possible context-dependent clinical relevance of RGS2 (Xu *et al*., 2023). However, the transcript-level expression pattern of RGS2 and its association with clinicopathological characteristics and survival outcomes in large-scale public datasets remain to be clarified.

Based on this evidence, this study aims to analyze RGS2 gene expression in ovarian cancer using publicly available RNA sequencing data from TCGA and GTEx. In addition to evaluating differences between tumor and normal tissues, this study

explores the association between RGS2 expression and clinicopathological characteristics as well as survival outcomes, including OS, DSS, PFI, and DFI. This exploratory transcriptomic analysis seeks to determine whether RGS2 downregulation represents a consistent molecular feature of ovarian cancer and to assess its potential clinical relevance.

METHODS

This study utilized secondary data retrieved from the University of California Santa Cruz (UCSC) Xena platform. Patient data for ovarian carcinoma were obtained from The Cancer Genome Atlas (TCGA) database via https://xenabrowser.net/, accessed in October 2023. The dataset included RNA sequencing-based gene expression data generated using the Illumina HiSeq 2000 platform, along with corresponding clinical data provided by the University of North Carolina TCGA cohort. To compare RGS2 gene expression between normal ovarian tissue and primary tumor tissue, additional gene expression data for normal ovarian samples were obtained from the GTEx database integrated within UCSC Xena. Gene expression data were obtained from the TCGA TARGET GTEx cohort available within the UCSC Xena platform. Expression values were provided as RSEM normalized counts and log2-transformed [log2(norm_count + 1)], allowing standardized comparison between tumor and normal tissue samples.

These samples were analyzed separately from the clinical baseline dataset, which consisted solely of ovarian cancer patients. Prior to analysis, all downloaded data were reviewed for completeness, and each variable was systematically coded to facilitate data processing. The exclusion criterion for this study was the absence of RGS2 gene expression data in the TCGA dataset. Only cases with available RGS2 expression and clinical profiles were included for further analysis. A total of 507 samples were included in the expression analysis, consisting of 419 primary ovarian carcinoma samples from TCGA and 88 normal ovarian tissue samples from GTEx.

Among the TCGA cohort, 308 patients had available clinical and survival information and were included in clinicopathological and survival analyses. Clinical variables with incomplete records were analyzed using available-case analysis. Cases with missing data were excluded only from the specific analysis requiring that variable, and no data imputation was performed. As a consequence, the total number of evaluable cases varied across clinicopathological variables depending on data completeness.

Statistical analyses were performed using statistical software. To compare RGS2 gene expression between normal ovarian tissues and primary tumor tissues, the Mann-Whitney U test was employed. Categorical variables did not meet the assumptions required for chi-square testing; therefore, Fisher's exact test and Kolmogorov-Smirnov test were used for statistical analysis.

To evaluate prognostic relevance, survival analyses were performed using the Kaplan-Meier method, with cumulative survival probabilities calculated for overall survival (OS), disease-specific survival (DSS), progression-free interval (PFI), and disease-free interval (DFI). Differences in survival outcomes between groups with high and low RGS2 expression were assessed using the log-rank test (Mantel-Cox). The expression of RGS2 was dichotomized into high and low categories based on the median value as a cutoff point. Given the exploratory nature of this transcriptomic study, survival associations were evaluated using univariate Kaplan-Meier analysis

without multivariable adjustment. No adjustment for multiple comparisons was performed because survival analyses were exploratory in nature. A p-value less than 0.05 was considered statistically significant for all analyses.

This study used publicly available de-identified data from TCGA and GTEx databases accessed through the UCSC Xena platform. No new human participants were recruited, and institutional ethical approval was therefore not required. Data usage complied with the access and usage policies of the respective databases

RESULTS AND DISCUSSIONS

Subject characteristics

Table 1 presents the baseline clinical characteristics of 308 ovarian cancer patients. The median age at diagnosis was 58 years (range: 30–87), with most patients (99.1%) presenting at an advanced stage. Histological grading revealed that high-grade tumors (G3) predominated (84.4%), while primary tumors accounted for 98.4% of the tissue samples.

Ovarian cancer is generally diagnosed in postmenopausal women. Although the median age in this study is slightly lower than the average age of diagnosis reported in the literature (63 years), the predominance of older age remains consistent with previous findings. Almost half of the women diagnosed with ovarian cancer are over 64 years old, and 25% of them are over 74 years old (Surveillance Research Program, 2026). Older patient age is associated with a worse prognosis, caused by more aggressive tumor biology, resistance to chemotherapy, comorbidities, decreased physiological reserves, and treatment disparities such as suboptimal therapy or low tolerance to chemotherapy (Ledermann *et al*., 2024; Perez-Fidalgo *et al.,* 2024).

The dominance of high-grade tumors in this study is consistent with international findings. Recent population-based studies have demonstrated that high-grade serous carcinoma (HGSC) is associated with significantly poorer survival than low-grade serous carcinoma (LGSC), reflecting its more aggressive biological behavior and advanced stage at diagnosis (Matsuo *et al*., 2024). Similarly, a recent large cohort study involving 2,074 patients with high-grade serous ovarian cancer (HGSC) demonstrated that stage III disease was the predominant stage at diagnosis, representing 69.2% of all cases, highlighting the aggressive clinical behavior and advanced presentation of HGSC (De Vitis *et al*., 2026). These findings underscore the aggressive nature of advanced ovarian cancer and highlight the urgent need for molecular biomarkers to improve early detection and risk stratification. Several factors contribute to the frequent diagnosis of ovarian cancer at advanced stages and with high-grade histology. Clinically, early-stage ovarian cancer often presents with vague and nonspecific symptoms, such as bloating, abdominal discomfort, or urinary frequency, which can easily be misinterpreted as benign gastrointestinal or urinary disorders (Kokori *et al*., 2025). As a result, diagnosis is often delayed until the disease has significantly progressed. Additionally, there is currently no effective and validated screening tool available for early detection in asymptomatic women. The examination of serum CA-125 levels and transvaginal ultrasound, although frequently used in practice, does not yet have adequate sensitivity and specificity to reliably detect early-stage cancer (Hong and Ding, 2025; Rampes *et al*., 2022).

From a biological perspective, HGSC, the most prevalent subtype of epithelial ovarian cancer, is known for its rapid proliferation, early peritoneal dissemination, and intrinsic genomic instability. These tumors often originate from the distal fallopian tube

epithelium and have characteristic TP53 mutations, contributing to their aggressive clinical behavior and poor prognosis (Cheng Z *et al.,* 2024). Because the ovaries are located deep within the pelvic cavity, tumors can grow substantially before producing noticeable symptoms, often delaying clinical presentation (Xiao *et al.,* 2024).

Survival analyses showed poor outcomes, 60.1% of patients were deceased at the time of analysis, 50.6% had died from disease-specific causes, 30.5% had experienced disease progression, and 33.1% had relapsed. These outcomes reflect the aggressive clinical course of ovarian cancer and underscore the need for improved biomarkers to support early diagnosis, risk stratification, and treatment monitoring. Ovarian cancer remains a significant health threat, with most cases diagnosed at advanced stages resulting in poor survival rates. Early detection is crucial, as the 5-year survival rate exceeds 93% for early-stage diagnoses but drops to approximately 20% for advanced-stage disease. Despite extensive research, no single biomarker has demonstrated adequate sensitivity and specificity for ovarian cancer diagnosis. Current diagnostic strategies rely on a combination of biomarkers, clinical symptoms, imaging, and algorithm-based tools to enhance diagnostic accuracy (Hong dan Ding., 2025). Advanced molecular approaches such as transcriptomics, proteomics, and bioinformatics are increasingly used to identify novel biomarkers, although substantial improvements over the current standards, CA125 and transvaginal ultrasound, remain elusive (Liu *et al*., 2021).

Table 1. Baseline demographic and clinical features of the study population

Variable	n (%) / Median (Min-Max)
Age	58 (30-87)
Stage	
Early	1 (0.3)
Advanced	305 (99.1)
Sample Type	
Primary Tumor	303 (98.4)
Recurrent Tumor	5 (1.6)
Grading	
G1	1 (0.3)
G2	37 (12.0)
G3	260 (84.4)
G4	1 (0,3)
Gx/b	6 (1,9)
Overall Survival	
Alive	123 (39.9)
Deceased	185 (60.1)
Disease Specific Survival	
Alive	128 (41.6)
Deceased	156 (50.6)
Progression-Free Interval	
Progressed	94 (30.5)
Not Progressed	214 (69.5)
Disease Free Interval	
No relapsed	47 (15.3)

Variable	n (%) / Median (Min-Max)
Relapsed	102 (33.1)
Total	**308**

Notes: Percentages may not total 100% because some clinical variables contained missing values in the TCGA dataset; Gx/b = unclassified or unavailable histological grade information in the TCGA dataset.

RGS2 expression in normal tissue compared to primary ovarian tumor tissue

Gene expression analysis revealed that RGS2 expression was significantly lower in primary ovarian tumor tissues (n=419) compared to normal ovarian tissues (n=88). The median RGS2 expression level was 11.435 (8.70–14.72) in normal ovarian tissue and 8.64 (0.00–12.03) in primary tumor tissue, demonstrating a significant reduction in tumor samples ($p<0.001$), as shown in Figure 1. This finding aligns with recent evidence indicating that RGS2 functions as a tumor suppressor by negatively regulating GPCR signaling, thereby influencing cell proliferation, migration, and survival (Xu *et al*., 2023; Yang *et al*., 2023). Epigenetic silencing mechanisms, such as histone deacetylation and DNA methylation, have been implicated in suppressing RGS2 expression in chemoresistant ovarian cancer cells (Cacan, 2017). Overexpression of RGS2 suppresses GPCR-mediated signaling involved in ovarian cancer progression, further supporting its tumor-suppressive function (Xu *et al*., 2023; Yang *et al*., 2023).

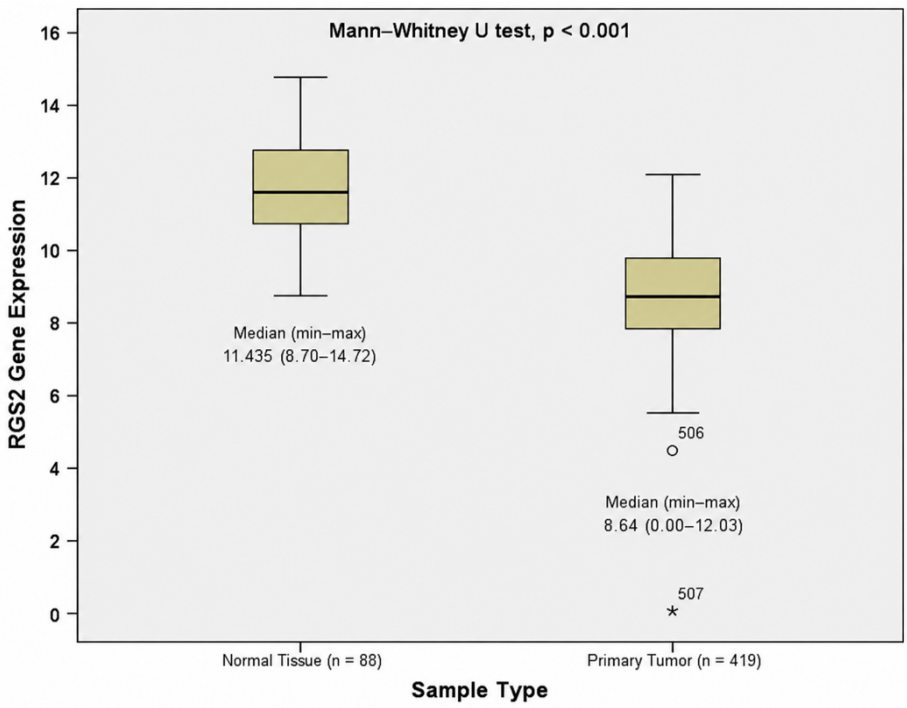

Fig. 1. Comparison of RGS2 gene expression between normal ovarian tissue and primary tumor tissue in ovarian cancer. A significant difference was observed in RGS2 expression between the two groups (p < 0,001)

However, whether downregulation of RGS2 directly causes carcinogenesis or is a consequence of tumor progression remains to be elucidated. It should also be acknowledged that comparisons between TCGA tumor samples and GTEx normal tissues may be influenced by technical variability inherent to publicly available

transcriptomic datasets. Functional studies suggest that low RGS2 expression may enhance cell survival and contribute to therapy resistance, but its prognostic significance appears to vary across tumor types and stages (McNabb *et al*., 2020).

RGS2 expression and clinical profile of ovarian cancer patients

Table 2 presents the distribution of clinical features based on RGS2 expression levels. No significant associations were observed between RGS2 expression and FIGO stage (p=1,000), histological grade (p=1,000), or sample type (p=0.371). Although there was a tendency for lower RGS2 expression in higher grade and advanced stage tumors, the differences were not statistically significant.

This result supports the notion that RGS2 downregulation may be an early molecular event in tumorigenesis rather than a determinant of disease aggressiveness. In contrast to breast cancer, where RGS2 expression was significantly associated with tumor grade (Wang *et al.,* 2018), this study found no such relationship in ovarian cancer. Similarly, Hu *et al.* (2021) identified other RGS family members, such as RGS10 and RGS16, but not RGS2, as being associated with tumor stage in ovarian cancer.

Table 2. Distribution of stage, grade, and sample type based on RGS2 gene expression levels in ovarian cancer patients

Variable		RGS2 Expression				*P-value*
		High		Low		
		n	%	n	%	
Stage*	Early	1	0.3	0	0.0	1.000
	Advanced	152	49.4	153	49,7	
Grade**	G1	1	0.3	0	0.0	1.000
	G2	19	6.17	18	5.9	
	G3	132	42.9	128	41.6	
	G4	0	0.0	1	0.3	
	Gx/b	1	0.3	5	1.6	
Sample Type*	Primary Tumor	153	49.7	150	48.7	0.371
	Recurrent Tumor	1	0.3	4	1.3	

Notes:*Fisher's exact test was used for the analysis; **The test was performed using the Kolmogorov-Smirnov test.

RGS2 gene expression and prognosis of ovarian cancer patients

Kaplan-Meier analysis (Fig. 2) revealed no significant difference in overall survival between patients with high and low RGS2 expression (5-year survival: 36% vs. 38%, p>0.05). This finding contrasts with previous studies showing that RGS2 expression is downregulated in breast cancer, colorectal cancer, and high-grade serous ovarian cancer (HGSOC), and that reduced RGS2 expression is associated with poorer overall survival (Ihlow *et al*., 2022; Liu *et al*., 2023; Yang *et al*., 2023). In breast cancer and HGSOC, low RGS2 expression was linked to more aggressive tumor behavior and shorter survival, especially in subgroups with no residual disease or early-stage tumors. Likewise, in colorectal cancer, low RGS2 levels were identified as an independent adverse prognostic factor.

The discrepancy between those results and the present findings may be attributed

to differences in tumor subtype, study design, population heterogeneity, or the molecular context in which RGS2 exerts its function. It is also possible that RGS2's impact on prognosis becomes more evident under specific clinical conditions, such as chemoresistance or BRCA mutation status, which were not assessed in this unstratified cohort (Pan and Xie, 2017).

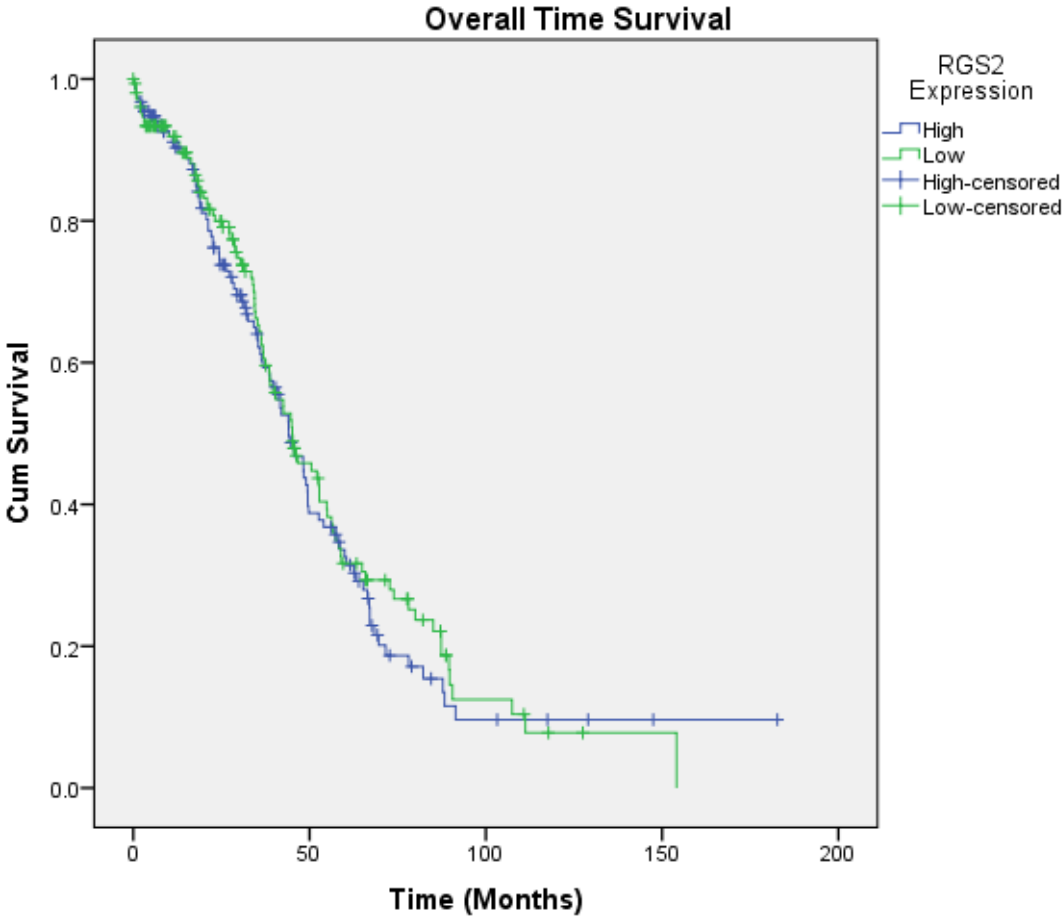

Fig. 2. Kaplan-Meier Curve of Overall Survival Based on RGS2 Gene Expression

Similarly, disease-specific survival (Fig. 3) did not differ significantly between high and low RGS2 expression groups (5-year DSS: 38% vs. 34%, $p > 0.05$). These findings suggest that RGS2 expression may not serve as a reliable prognostic marker for DSS in unstratified ovarian cancer populations. This result differs from the study by Jiang *et al.* (2010), which reported that reduced RGS2 expression was significantly associated with poorer disease-specific survival in colorectal cancer. Such discrepancies may reflect differences in tumor biology, molecular subtypes, and clinical context, indicating that the prognostic role of RGS2 could be cancer-type specific.

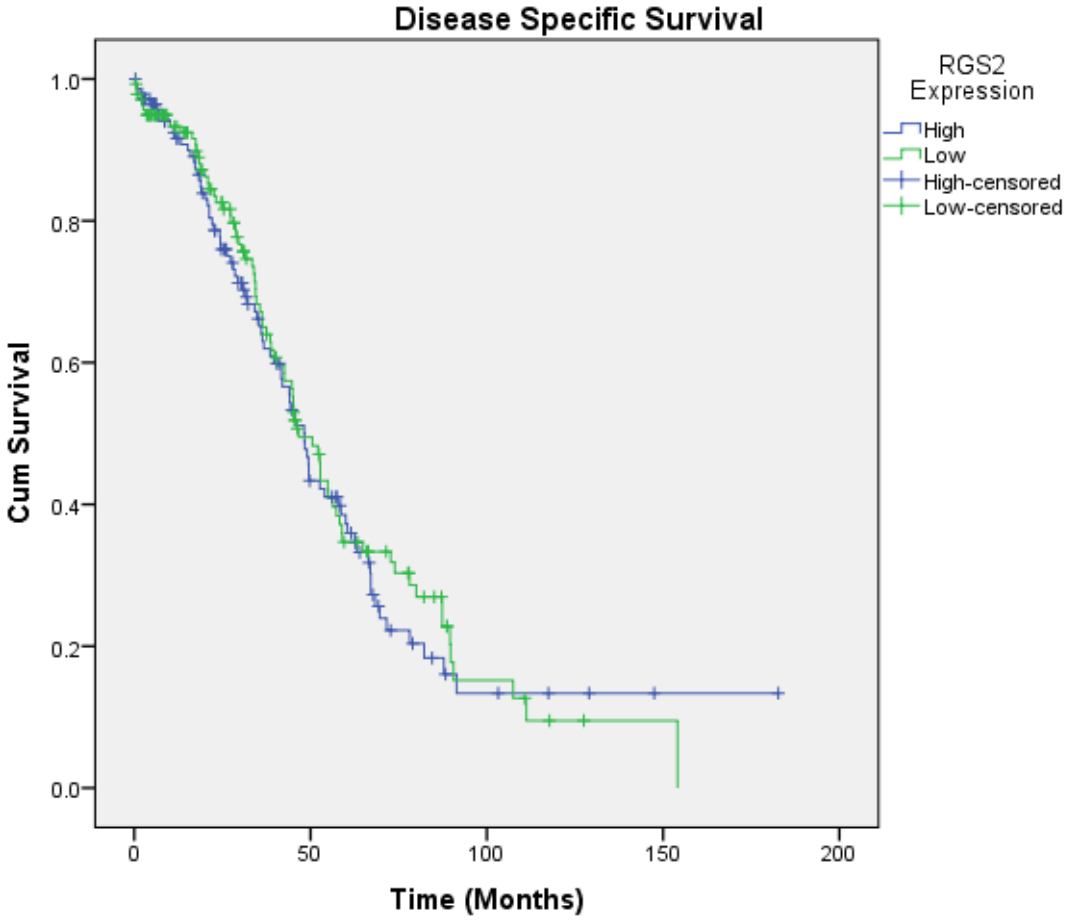

Fig. 3. Kaplan-Meier Curve of Disease-Specific Survival Based on RGS2 Gene Expression

In this study, patients with low RGS2 expression demonstrated a slightly better 5-year progression-free interval of 15% compared to 12% in those with high expression. However, the difference was not statistically significant ($p > 0.05$), indicating no clear prognostic value of RGS2 expression in predicting disease progression (Fig. 4). These findings differ from those reported by Ihlow *et al.* (2022), where low RGS2 protein expression was associated with poorer progression-free survival in high-grade serous ovarian cancer (HGSOC), particularly in patients with lower FIGO stage and no residual tumor burden. Although our study did not demonstrate a significant association between RGS2 mRNA expression and progression-free interval (PFI), this finding contrasts with the study by Ihlow *et al.* (2022), which reported a significant negative impact of low RGS2 protein expression on PFI, particularly in patients with lower FIGO stages and no residual tumor burden. The discrepancy may be attributed to differences in the level of biological analysis. While our analysis was based on mRNA expression data, Ihlow *et al.* (2022) examined RGS2 at the protein level. Such divergence is not uncommon, as mRNA levels do not always correlate directly with protein abundance due to various post-transcriptional and translational regulatory mechanisms (Buccitelli and Selbach, 2020). This highlights the need for integrative transcriptomic-proteomic studies to fully elucidate the functional role of RGS2 in ovarian cancer progression.

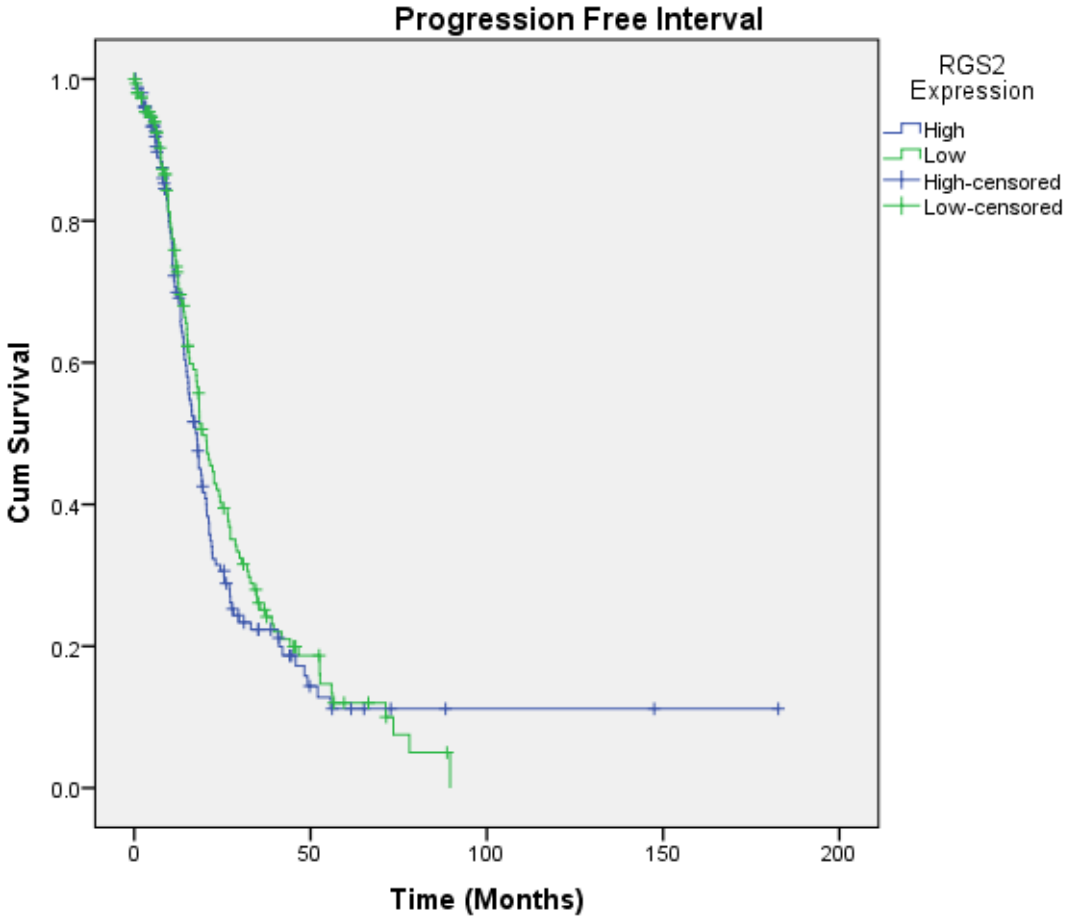

Fig. 4. Kaplan-Meier Curve of Progression-Free Interval Based on RGS2 Gene Expression

Disease-free interval (DFI) analysis was conducted to evaluate the relationship between RGS2 gene expression and recurrence risk in ovarian cancer patients. Kaplan-Meier curves (Fig. 5) showed that the 5-year cumulative probability of remaining recurrence-free was approximately 15% in the low RGS2 expression group, compared to 14% in the high-expression group. Although the low-expression group appeared to demonstrate slightly better recurrence-free survival in the short term, the difference between the groups was not statistically significant ($p > 0.05$).

These findings indicate that RGS2 expression does not significantly influence the likelihood of disease recurrence in ovarian cancer. While RGS2 has been implicated in regulating cell proliferation, migration, and GPCR-mediated signaling pathways (Xu *et al*., 2023; Yang *et al*., 2023), its prognostic utility for predicting tumor relapse remains limited in this cohort. The absence of a statistically significant association may suggest that recurrence in ovarian cancer is influenced more strongly by other clinical and molecular factors, including residual disease after cytoreductive surgery, BRCA mutation status, response to platinum-based chemotherapy, and homologous recombination deficiency (HRD) (Hong dan Ding, 2025; Cheng Z *et al*., 2024).

Previous studies have shown that epigenetic silencing of RGS family members, including RGS2 and RGS10, may contribute to therapy resistance and disease progression (Cacan, 2017). However, these effects may not directly translate to recurrence risk without further context, such as treatment exposure or tumor subtype.

For instance, in high-grade serous ovarian cancer, Xu *et al.* (2023) reported that reduced RGS2 expression correlated with platinum resistance, which could indirectly affect recurrence rates. Nonetheless, such associations were not evident in the broader, unstratified patient population assessed in this study.

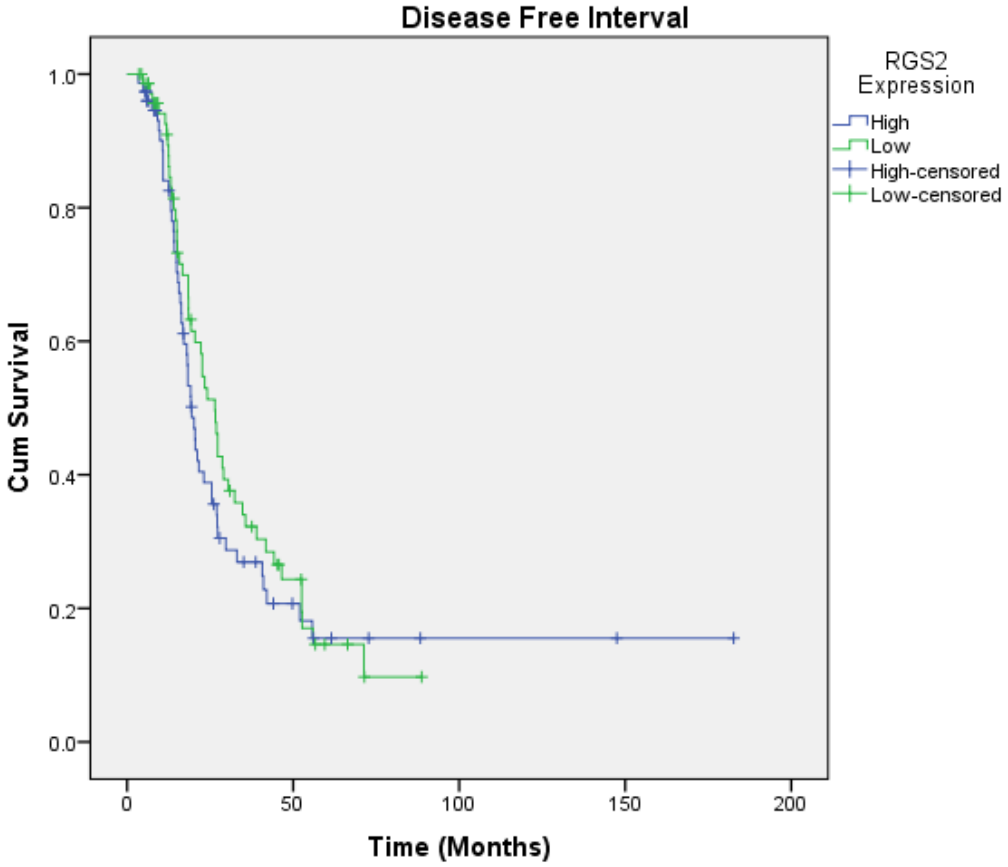

Fig. 5. Kaplan-Meier Curve of Disease-Free Interval Based on RGS2 Gene Expression

Overall, the current findings suggest that RGS2 expression alone is insufficient as a standalone biomarker for predicting long-term recurrence in ovarian cancer patients. Further investigation is needed to determine whether RGS2 has predictive value within specific molecular subtypes or in conjunction with other biomarkers.

CONCLUSIONS

The results of this study indicate that RGS2 gene expression is significantly lower in ovarian cancer tissue compared to normal ovarian tissue, suggesting that reduced RGS2 expression may represent a consistent molecular alteration associated with ovarian cancer. This differential expression suggests that RGS2 downregulation may be associated with molecular changes observed during ovarian cancer development. However, no meaningful associations were found between RGS2 expression and clinical indicators such as tumor grade, disease stage, or patient prognosis. The lack of prognostic significance implies that RGS2 alone may not serve as a reliable biomarker for predicting disease severity or outcomes in ovarian cancer. These findings highlight the need for further investigation through prospective clinical studies involving larger

and more diverse patient populations. Future research should consider integrating RGS2 expression analysis with molecular subtype classification and treatment response data to better understand its role in ovarian cancer biology and its potential as a therapeutic target.

ACKNOWLEDGMENTS

The author would like to express sincere gratitude to The Cancer Genome Atlas (TCGA) and UCSC Xena platforms for providing open access to the genomic and clinical datasets used in this study. Appreciation is also extended to the institutions and data contributors involved in generating and maintaining these valuable resources. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST

The authors declare that they have no conflict interest.

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