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Pan-cancer analyses reveal the prognostic and immune relevance of OAS1 and its pro-migratory role in cervical cancer

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Abstract

Objective:

To systematically investigate the pan-cancer expression, prognostic significance, immune relevance, and functional role of OAS1 in cervical cancer.

Methods:

OAS1 expression, genetic alterations, prognosis, cancer stemness, RNA modification, immune infiltration, and immunotherapy-related indicators were analyzed using TCGA, GTEx, HPA, GEPIA3, SangerBox, cBioPortal, TIMER3.0, and CAMOIP databases. GO and KEGG enrichment analyses were performed for OAS1 co-expressed genes. In cervical cancer, OAS1 expression was validated by immunohistochemistry and Western blotting. Stable OAS1 knockdown and overexpression HeLa cell lines were established to evaluate migration, invasion-related phenotypes, and reactive oxygen species levels. Single-cell analyses were used to characterize the cell-type-specific expression and distribution of OAS1.

Results:

OAS1 was upregulated at both mRNA and protein levels in multiple cancers, particularly cervical cancer. Its expression was associated with tumor stage, metastasis, genetic alterations, prognosis, cancer stemness, RNA modification-related genes, immune infiltration, TMB, MSI, and immune checkpoint molecules in a cancer type-dependent manner. OAS1 co-expressed genes were mainly enriched in type I interferon signaling, antiviral response, and innate immune pathways. In cervical cancer, OAS1 was highly expressed in tumor tissues. OAS1 overexpression promoted HeLa cell migration and increased ROS levels, whereas OAS1 knockdown suppressed migration/invasion-related phenotypes and reduced ROS levels. Single-cell showed that OAS1 was mainly expressed in epithelial/tumor cells and monocyte/macrophage populations.

Conclusion:

OAS1 may serve as a diagnostic, prognostic, and immune-related biomarker across cancers. In cervical cancer, OAS1 may promote malignant phenotypes by enhancing migration, invasion-related behavior, and oxidative stress, suggesting its potential as a therapeutic target.

Keywords: cervical cancer; pan-cancer analysis; biomarker; OAS1; tumor immune microenvironment

INTRODUCTION

Cancer is a highly complex and heterogeneous disease involving molecular alterations at genomic, epigenomic, transcriptomic, and proteomic levels [1]. Despite recent advances in targeted therapy and immunotherapy, cancers exhibit both shared molecular features and tumor-specific differences in mechanisms, immune microenvironments, and therapeutic responses [2]. Systematic characterization of key molecules across cancer types is essential for understanding tumorigenesis and optimizing precision treatment [3].

Tumor biomarkers are critical for cancer screening, diagnosis, prognosis, and treatment prediction. While ctDNA [4], CEA, and PSA [5–6] are widely used, novel biomarkers with broad applicability remain an important pursuit in precision oncology.

The 2'-5'-oligoadenylate synthetase (OAS) family—OAS1, OAS2, OAS3, and OASL—are interferon-induced enzymes central to innate antiviral immunity [7]. Upon activation by viral double-stranded RNA, OAS enzymes synthesize 2'-5'-linked oligoadenylates (2-5A), which activate RNase L to degrade viral and host single-stranded RNA, inhibiting protein synthesis and viral replication [8–9].

OAS1, encoding multiple isoforms and widely expressed in mammalian tissues [10], has canonical antiviral roles through the OAS/RNase L pathway. Beyond this, OAS1 binds specific mRNAs (e.g., IFN β AU-rich elements) to extend mRNA half-life and maintain expression [11]. It also selectively preserves translation of host defense proteins and potently inhibits SARS-CoV-2 via RNase L-dependent mechanisms [12–13].

Increasing evidence links OAS1 to cancer. It may act as a tumor-promoting gene in breast and pancreatic cancers [14–15], and its expression correlates with prognosis in multiple malignancies. In gastric cancer, OAS1 may influence outcomes via inflammation and proliferation pathways [16]. OAS1 expression also correlates with immune checkpoint genes and tumor mutational burden, suggesting involvement in immune microenvironment regulation [17]. In lung adenocarcinoma, OAS1 overexpression associates with poor prognosis and metastasis; its knockdown suppresses proliferation and migration in lung and prostate cancer cells [18].

Although OAS1 is a potential prognostic biomarker in certain cancers, pan-cancer

analyses remain limited, and its broader biological roles and mechanisms in tumorigenesis and immune regulation are incompletely understood. A systematic pan-cancer analysis is needed to evaluate OAS1 expression, prognostic value, genetic/epigenetic alterations, immune infiltration associations, and functional pathways, clarifying its general and context-dependent roles and providing a basis for its application as a biomarker and therapeutic target.

MATERIALS AND METHODS

1. Pan-cancer analysis of OAS1

OAS1 mRNA and protein expression were analyzed using TCGA, GTEx, HPA, GEPIA3, and SangerBox databases. Differential expression of OAS1 between tumor and normal tissues was evaluated across multiple cancer types, and its association with clinical stage, metastasis, age, and sex was further assessed. Protein expression and immunohistochemical staining images were obtained from the HPA database.

2. Genetic alteration and prognostic analysis

Genetic alterations of OAS1, including mutation frequency, mutation types, copy number alterations, and mutation sites, were analyzed using cBioPortal, TIMER3.0, SangerBox, and CAMOIP. The prognostic value of OAS1 was evaluated using SangerBox and GEPIA3. Overall survival, disease-specific survival, disease-free survival, and progression-free survival were analyzed by Cox regression and Kaplan–Meier methods.

3. Stemness, RNA modification, and functional enrichment analyses

Correlations between OAS1 expression and cancer stemness indices or RNA modification-related genes were analyzed using SangerBox. OAS1 co-expressed genes were obtained from cBioPortal, and overlapping genes across representative cancer types were identified. GO and KEGG enrichment analyses were performed to explore the biological functions and pathways associated with OAS1.

4. Immune infiltration analysis

The relationship between OAS1 expression and the tumor immune microenvironment was analyzed using SangerBox. Correlations between OAS1 and StromalScore, ImmuneScore, ESTIMATEScore, and multiple immune cell types, including CD4⁺ T cells, CD8⁺ T cells, B cells, neutrophils, macrophages, and dendritic cells, were evaluated using Pearson correlation analysis.

5. Experimental validation in cervical cancer

The study protocol and the use of human cervical cancer tissue samples were reviewed and approved by the Ethics Committee of the Second Affiliated Hospital of Dalian Medical

University (approval no. JW2026-028-01). All procedures involving human participants and human tissue samples were performed in accordance with the relevant institutional and national guidelines and regulations and with the Declaration of Helsinki. Written informed consent for participation in the study and for the collection and use of tissue samples was obtained from all participants prior to their inclusion in the study.

6. Cell migration and ROS assays

Wound healing and Transwell assays were performed to evaluate the effects of OAS1 on HeLa cell migration and invasion-related phenotypes. Reactive oxygen species levels were detected using a ROS fluorescent probe and compared among control, OAS1 knockdown, and OAS1 overexpression groups.

7. Single-cell analysis

Cervical cancer single-cell RNA sequencing datasets were obtained from GEO, including GSE208653. Data normalization, dimensionality reduction, clustering, batch correction, and cell annotation were performed using R software.

8. statistical analysis

Statistical analyses were performed using SPSS 26.0, GraphPad Prism 9.0, R software, ImageJ, and QuPath. Data are presented as mean $\pm$ standard deviation. Student's t-test, one-way ANOVA, χ^2 test, nonparametric tests, Cox regression, and Pearson correlation analysis were used as appropriate. A two-sided P value < 0.05 was considered statistically significant.

RESULTS

1. OAS1 expression is upregulated in multiple cancer types

Based on HPA, GTEx, and TCGA database analyses, OAS1 showed the highest expression in the esophagus among normal tissues, followed by the spleen, liver, and colon (Figure 1A). Among tumor tissues, OAS1 expression was highest in cervical cancer, followed by head and neck squamous cell carcinoma and colon adenocarcinoma (Figure 1B).

Using GEPIA 3.0 to compare expression between 33 tumor types and corresponding normal tissues, OAS1 was significantly upregulated in 28 cancer types, including ACC, BLCA, and CESC, downregulated in DLBC and KICH, and showed no significant change in MESO, THYM, and UVM, indicating clear cancer-type specificity (Figure 1C); all cancer abbreviations are listed in Table S1. Stratified analyses of tumor progression revealed that OAS1 expression increased with tumor stage in the KIPAN cohort (Figure S1A); OAS1 expression was significantly higher in M1-stage tissues than in M0-stage tissues in KIPAN, KIRC, and other cancers (Figure S1B); OAS1 expression increased with lymph node stage progression in LUAD,

PRAD, and other cancers (Figure S1C), suggesting that elevated OAS1 expression is closely associated with tumor progression, distant metastasis, and lymph node metastasis.

Immunohistochemistry results from the HPA database confirmed that OAS1 protein was significantly overexpressed in 15 cancer types (Figure 2), consistent with the mRNA expression trends.

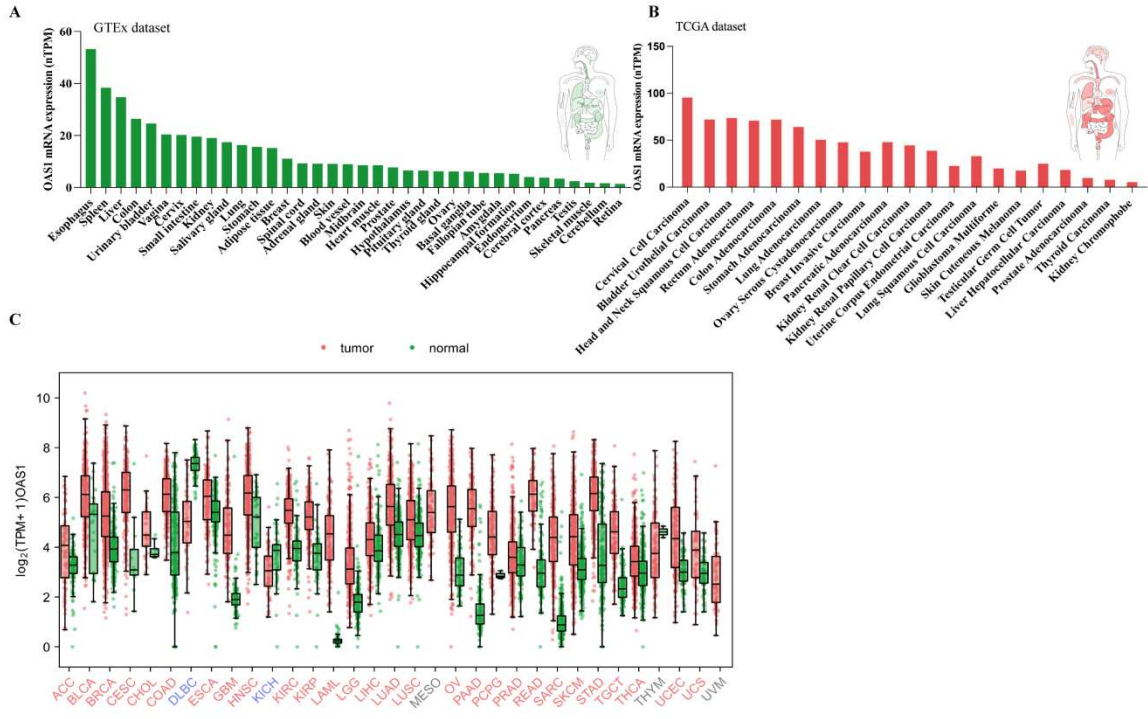


Figure 1. Pan-cancer OAS1 expression.

(A) OAS1 mRNA in HPA/GTEx normal tissues. (B) OAS1 mRNA in TCGA tumors via HPA. (C) GEPIA3 tumor–normal comparison across 33 cancers; red/blue, up-/downregulated.

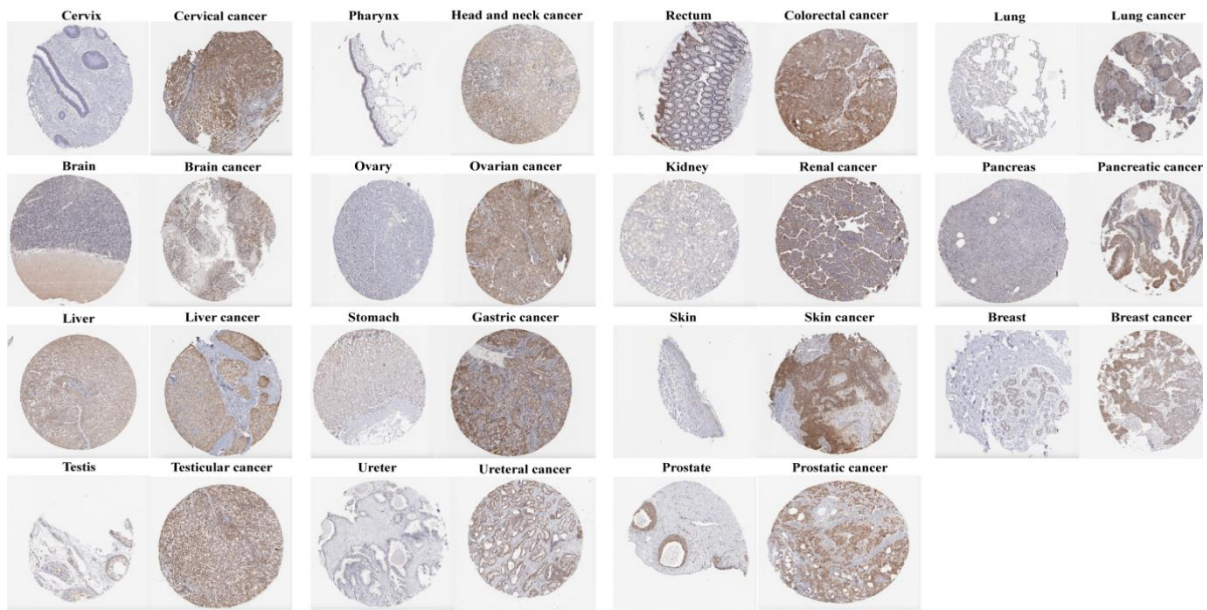


Figure 2. HPA IHC of OAS1 protein in corresponding normal and cancer tissues; brown, OAS1 staining.

2. OAS1 genetic alterations are associated with the development and progression of multiple cancers

Pan-cancer database analyses revealed that OAS1 harbors genetic alterations across multiple cancer types. The highest mutation frequency was observed in lung cancer, followed by non-melanoma skin cancer, medulloblastoma, and UCEC (Figure 3A). TIMER 3.0 analysis further validated that UCEC had the highest proportion of OAS1 mutations, followed by SKCM, READ, KICH, and other cancers (Figure 3B).

SangerBox analysis demonstrated that missense mutations were the predominant type of OAS1 mutation in tumors (Figure 3C), with mutation sites predominantly enriched in the C-terminal OAS1_C functional domain, while the N-terminal domain harbored fewer mutations (Figure 3D). The R361 site was identified as a core mutational hotspot; mutations at this site may alter OAS1 protein function and hold potential research and biomarker value. Additionally, high-frequency OAS1 amplification was observed in medulloblastoma and endometrioid carcinoma, while high-frequency deep deletion occurred in ovarian cancer (Figure 3A). Correlation analyses across multiple cancer types confirmed that increased OAS1 copy number was significantly associated with elevated mRNA expression in various tumors (Figure 3E), indicating that copy number variation is an important genetic mechanism underlying OAS1 upregulation. In summary, OAS1 genetic alterations are widely involved in the development and progression of multiple cancers and are closely associated with tumor molecular heterogeneity.

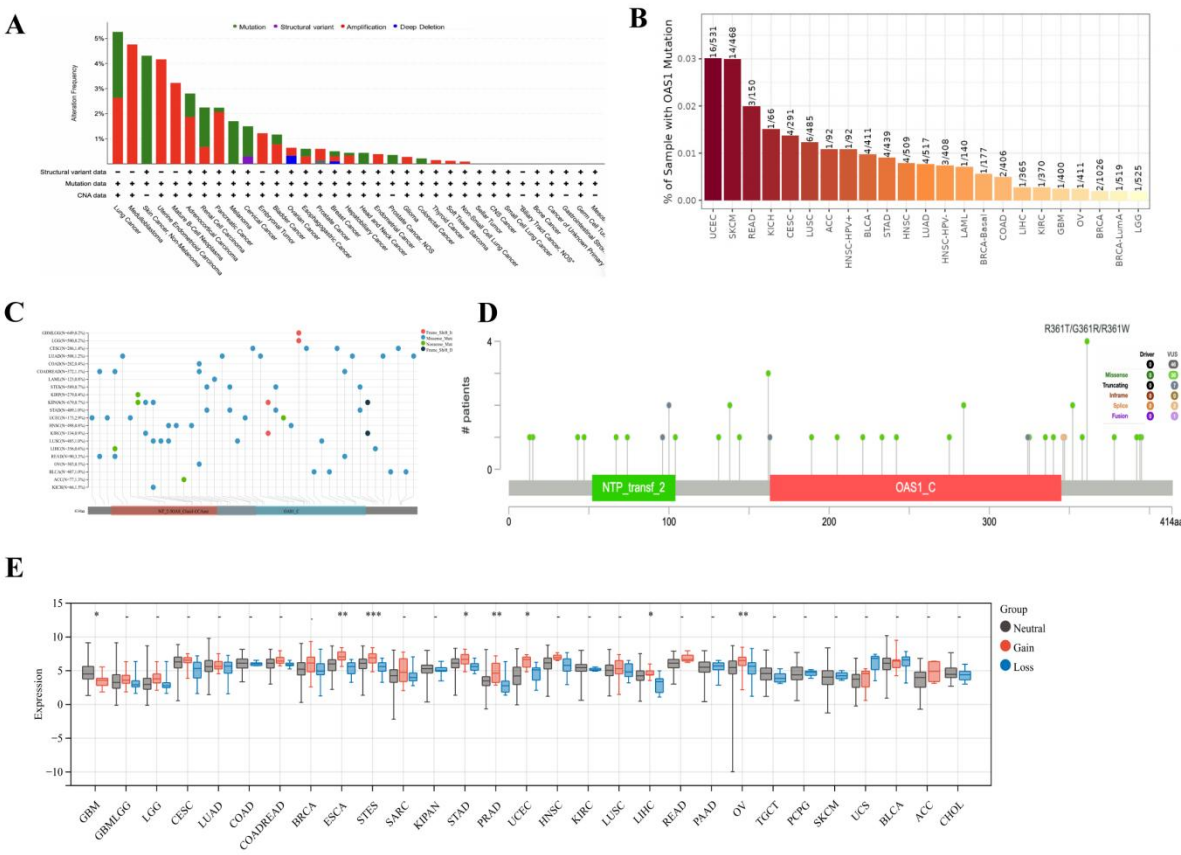


Figure 3. Pan-cancer genomic alterations of OAS1.
(A–E) Alteration frequency, mutation type and domain, and variant expression from cBioPortal, TIMER3.0, and SangerBox.

3. OAS1 expression is correlated with prognosis in multiple tumor types

SangerBox forest plots showed that high OAS1 expression was significantly associated with shorter overall survival in 10 cancer types, including GBMLGG, LGG, and PAAD (Figure 4A); however, it was associated with reduced mortality risk in 5 cancer types such as BLCA, SKCM, and MESO, demonstrating pronounced cancer-type specificity (Figure 4B).

Survival curves generated by GEPIA 3.0 validated that high OAS1 expression indicated poor overall survival prognosis in ACC, LGG, LIHC, and other tumors (Figure 4B). Multidimensional prognostic analyses confirmed that elevated OAS1 expression significantly increased the disease-specific mortality risk (Figure S2A), recurrence-free risk (Figure S2B), and disease progression risk (Figure S2C) in certain tumor types.

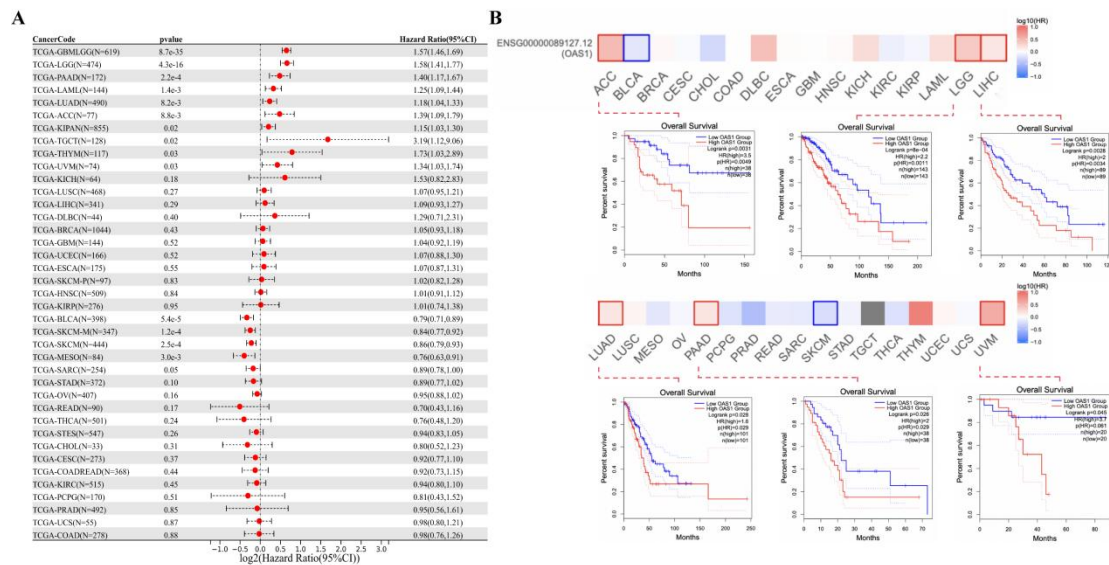


Figure 4. Pan-cancer association between OAS1 expression and overall survival.
 (A) Forest plot showing univariate Cox associations between OAS1 expression and overall survival across cancer types. (B) Pan-cancer survival summary and representative Kaplan–Meier curves generated using GEPIA3.0.

4. OAS1 is associated with cancer stemness and RNA modifications in multiple cancers

Using six classical stemness indices, we analyzed the correlation between OAS1 and tumor stemness. The results revealed significant cancer-type specificity: high OAS1 expression enhanced cancer stem cell characteristics in some tumors, while it suppressed stemness phenotypes in others (Figure 5A-F), suggesting that its regulatory role depends on the tumor molecular background.

RNA modification is an important mode of epitranscriptomic regulation. We further analyzed the correlation between OAS1 and m¹A, m⁵C, and m⁶A modification enzymes. OAS1 was positively correlated with the expression of RNA modification enzymes in the vast majority of tumors, with a negative correlation observed only in DLBC (Figure 5G).

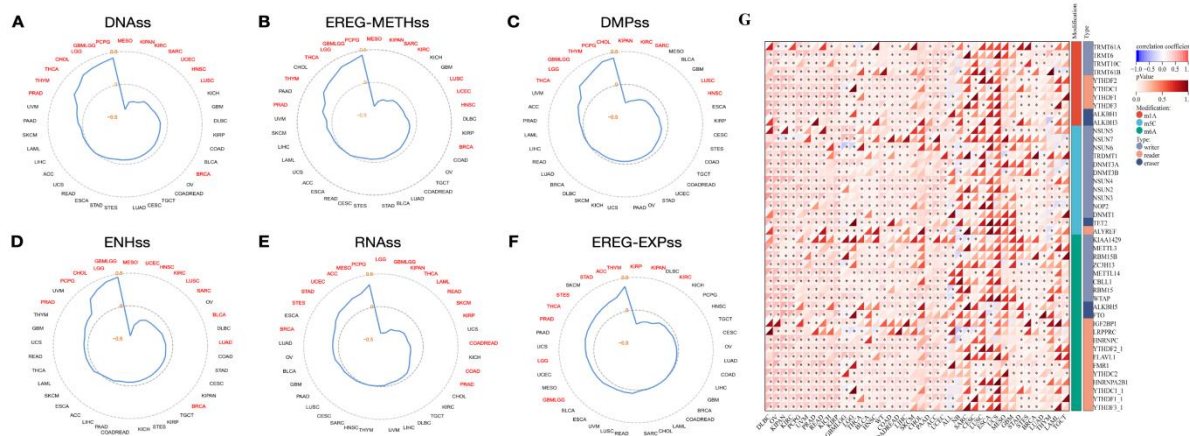


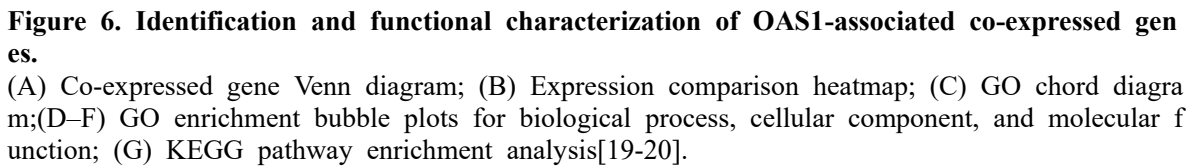
Figure 5. OAS1 correlation with stemness, RNA modifications

(A-F) Cancer stemness index radar plots; (G) RNA modification gene correlation heatmap

5. Enrichment analysis of OAS1 co-expressed genes across multiple tumors

We selected six tumor types characterized by high OAS1 expression, prominent stemness features, and poor prognosis, and screened their co-expressed genes for enrichment analysis. Venn diagram analysis identified five overlapping co-expressed genes: OAS2, ISG15, IFI44, IFI6, and OAS3 (Figure 6A). A heatmap confirmed that these genes were generally highly expressed across multiple cancer types (Figure 6B), synergistically contributing to tumor progression.

GO enrichment analysis revealed that the co-expressed genes were mainly enriched in type I interferon signaling pathways, antiviral responses, immune responses, etc., and were localized in the cytoplasm and nucleoplasm, with functions such as oligoadenylate synthetase activity and RNA binding (Figures 6C). KEGG analysis showed that the genes were primarily involved in viral infection and innate immune-related pathways (Figure 6D-G), indicating that OAS1 and its co-expressed genes play a core role in regulating tumor innate immunity and the immune microenvironment. Additionally, OAS1 expression exhibited population differences, being significantly associated with patient age and sex in certain cancer types (Figures S3A, S3B).



We analyzed the association between OAS1 and tumor microenvironment scores. The results showed that OAS1 expression was significantly positively correlated with stromal score, immune score, and ESTIMATE score in the majority of tumors, promoting stromal remodeling and immune infiltration; in a few cancer types, negative correlations were observed, demonstrating cancer-type specificity (Figure 7A-C).

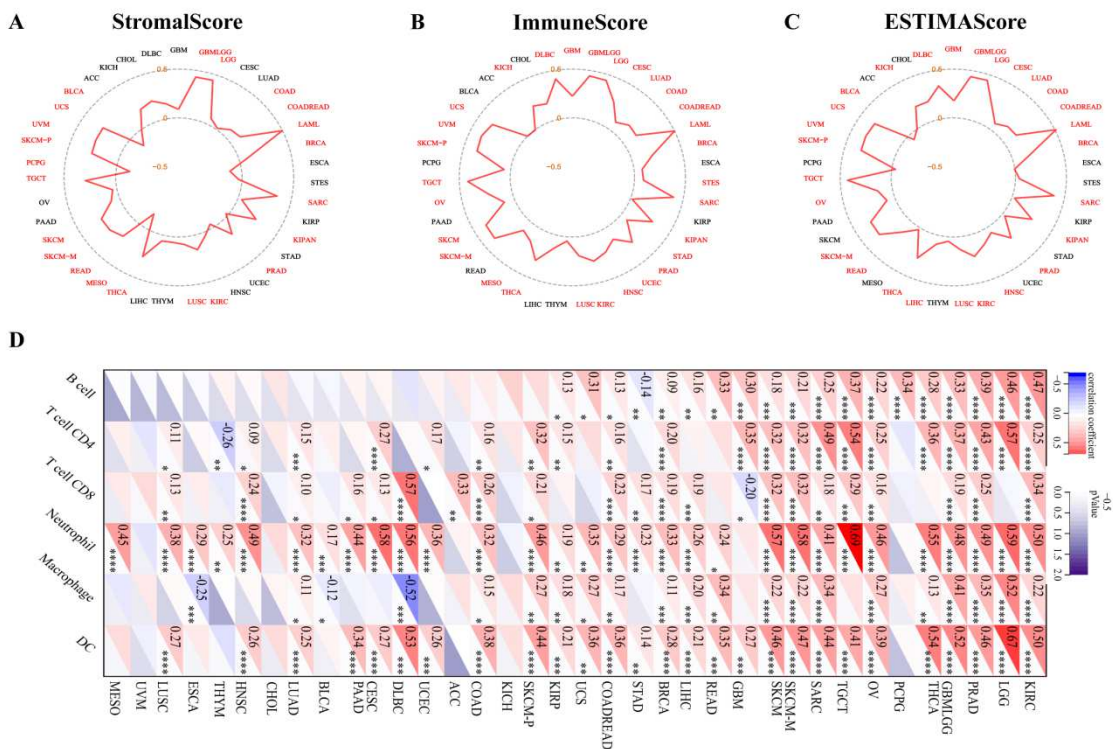


Figure 7. Association of OAS1 expression with the tumor immune microenvironment. (A-C) Immune/stromal score radar plots; (D) Immune cell infiltration correlation heatmap. Red indicates $p < 0.05$. Data: SangerBox, GEPIA3.0.

7. OAS1 is associated with immunotherapy-related indicators and immune checkpoint molecules

To explore the relationship between OAS1 and immunotherapy, we analyzed its correlation with TMB, MSI, NEO, and immune checkpoint genes. The results showed that OAS1 was positively correlated with TMB and MSI in some renal cancers, potentially enhancing tumor immunogenicity, whereas negative correlations were found in other tumors, reflecting cancer-type differences; no significant correlation was observed between OAS1 and NEO in any cancer type (Figure 8A-C).

Immune gene analysis revealed that OAS1 was simultaneously positively correlated with inhibitory checkpoint genes such as PDCD1 and CTLA4, as well as immune activation genes like CXCL10 and IFNA, across multiple cancer types (Figure 8D), suggesting that tumors with

high OAS1 expression exhibit features of abundant immune infiltration but with concurrent upregulation of immunosuppressive signals.

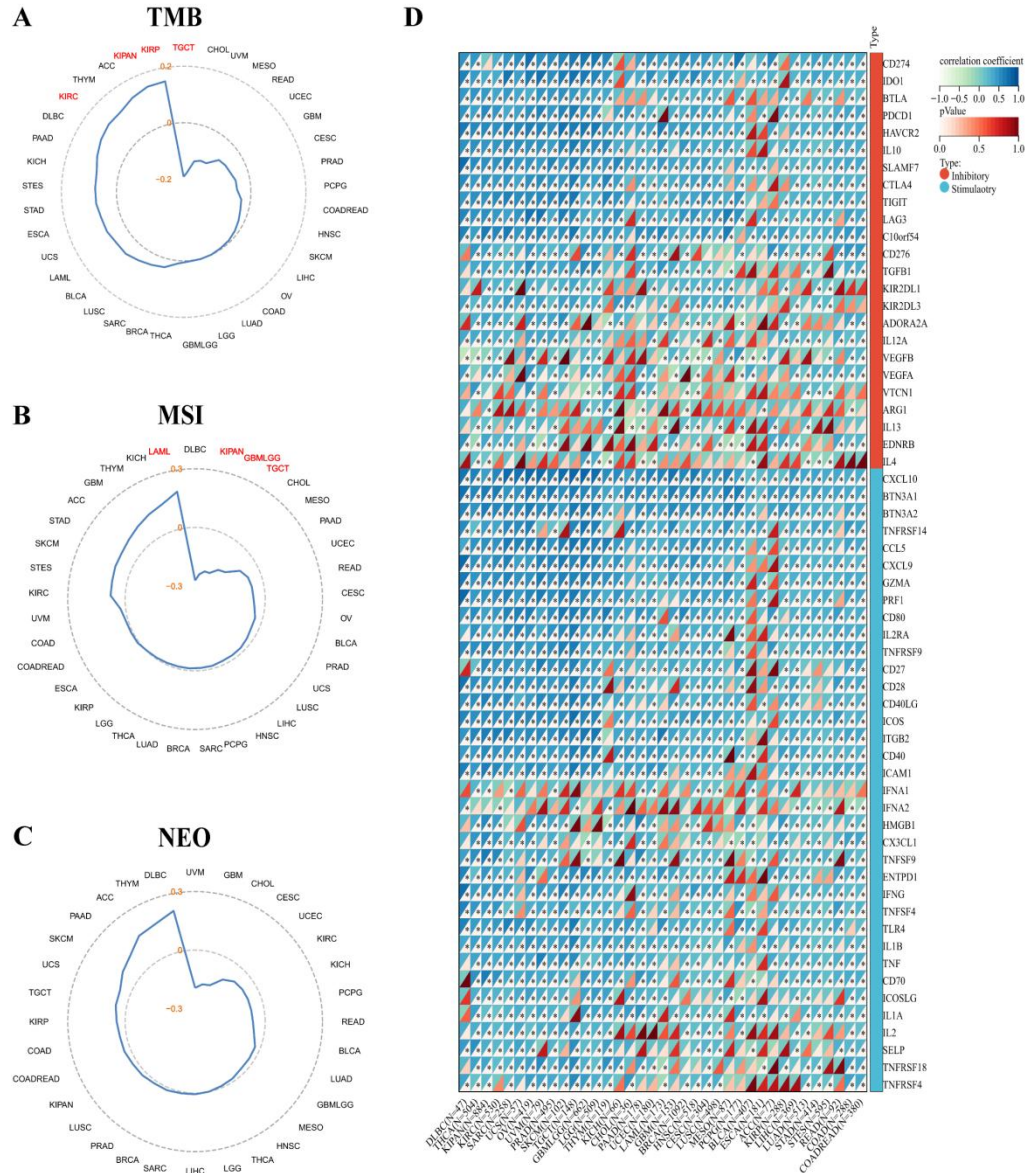


Figure 8. Pan-cancer immune correlations of OAS1
(A-C) OAS1 correlation with tumor immunogenicity (TMB, MSI, NEO) ; (D) immune checkpoints across cancers .

8. Single-cell transcriptomic analysis reveals the cellular origin and expression characteristics of OAS1 in cervical cancer

Based on cervical cancer single-cell transcriptomic data, we characterized OAS1 expression at the cellular level. Clustering analysis of samples from two cervical squamous cell carcinomas and one cervical adenocarcinoma identified 15 cell subpopulations (Figure 9A). Cell annotation

and UMAP visualization showed that OAS1 was predominantly highly expressed in cervical tumor epithelial cells, with high expression also observed in monocytes/macrophages (Figure 9B). OAS1-positive cells were mainly enriched in the monocyte/macrophage population, with a small portion distributed in tumor epithelial cells (Figure 9C-D). In summary, OAS1 acts on both cervical tumor cells and immune cells, participating in malignant regulation and immune microenvironment remodeling.

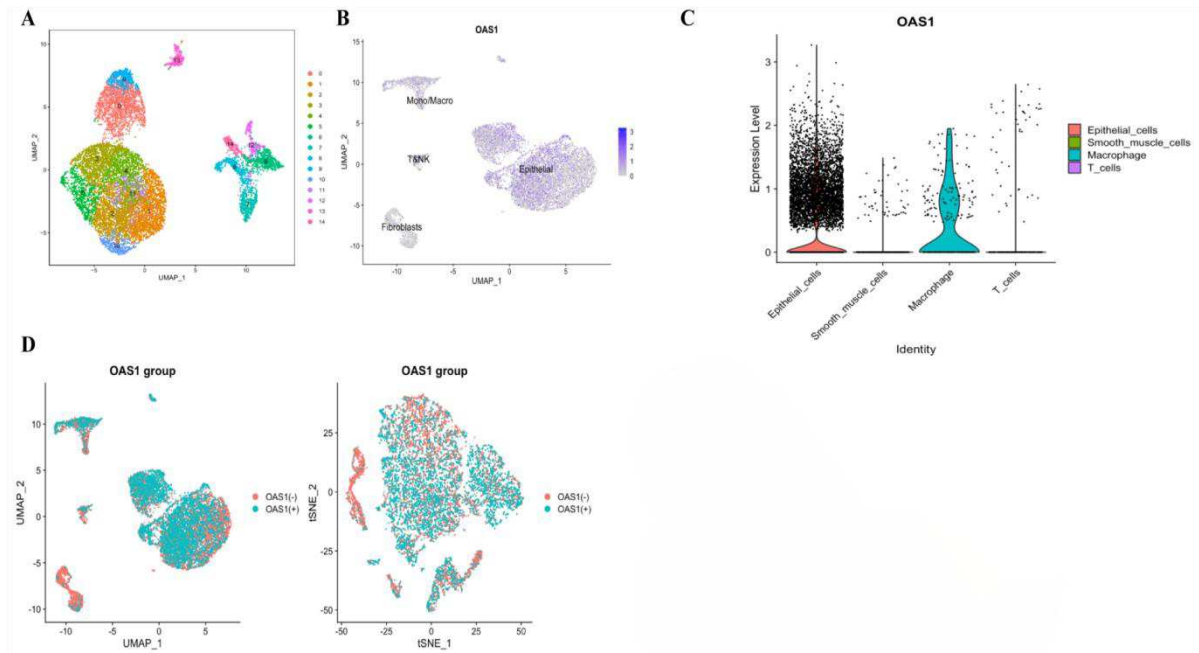


Figure 9. cervical cancer transcriptomic characteristics of OAS1

(A) UMAP visualization of the single-cell transcriptomic landscape, with cells colored according to unsupervised clusters. (B) Feature plot showing the distribution and expression intensity of OAS1 across the major cell populations. (C) Violin plot comparing OAS1 expression levels among epithelial cells, smooth muscle cells, macrophages, and T cells.

(D) UMAP and t-SNE visualizations showing the distribution of OAS1-positive [OAS1(+)] and OAS1-negative [OAS1(-)] cells across the single-cell landscape

9. OAS1 is highly expressed in human cervical cancer tissues, and OAS1 knockdown and overexpression HeLa cell lines were successfully established

Based on the pan-cancer analysis, we validated the expression characteristics of OAS1 in cervical cancer. Immunohistochemistry results showed that OAS1 staining intensity was significantly higher in cervical cancer tissues than in adjacent normal tissues (Figures 10A-B); Western blotting confirmed that OAS1 protein expression was significantly upregulated in cervical cancer tissues (Figures 10C-D).

For functional experiments, we established stable OAS1 knockdown and overexpression

cell lines in HeLa cells. Western blotting verified the successful construction of the cell models (Figures 10E-F), and GFP fluorescence detection confirmed good lentiviral transduction efficiency (Figure 10G), providing reliable models for subsequent in vitro functional studies.

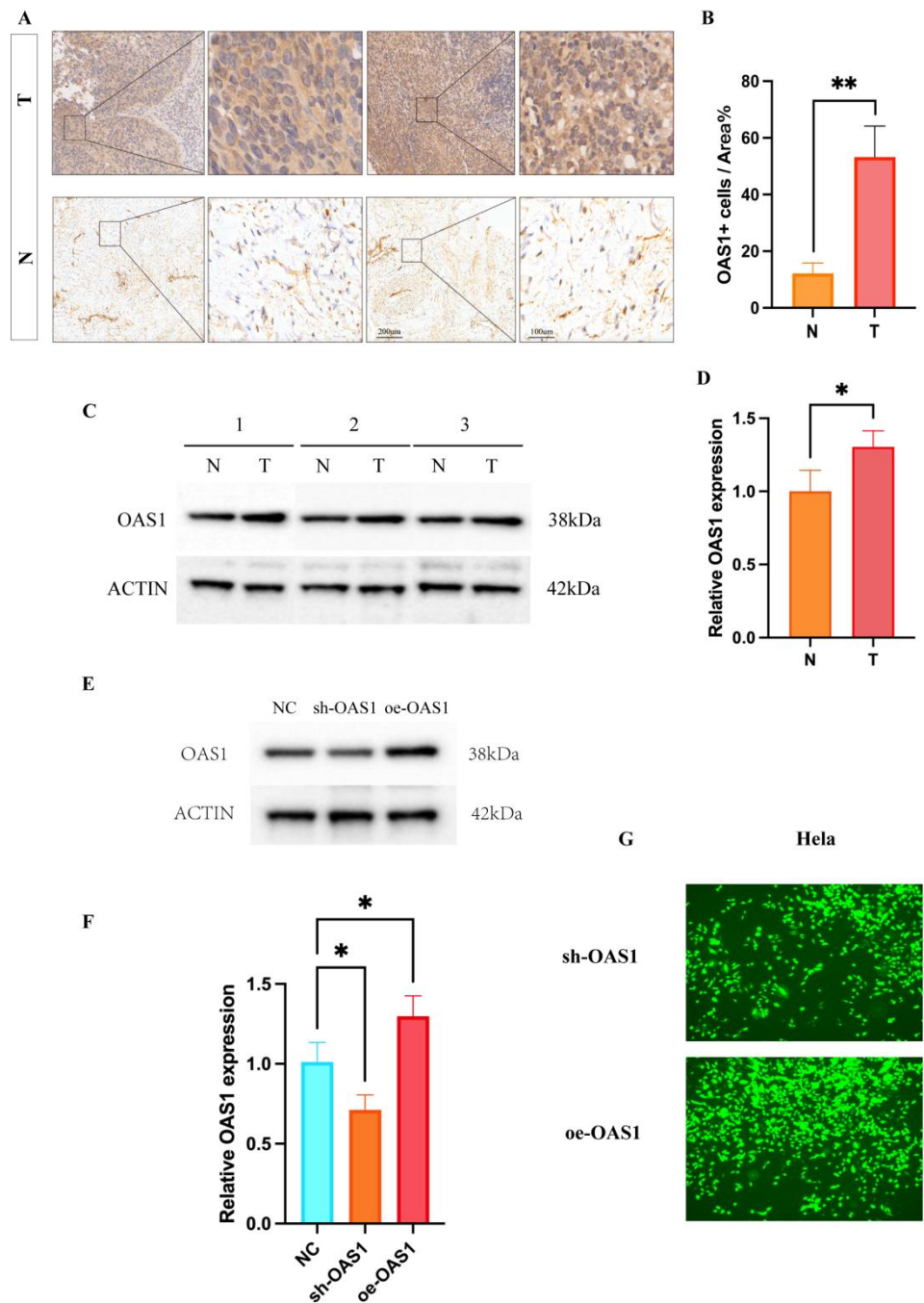


Figure 10. OAS1 overexpression in cervical cancer and knockdown/overexpression cell lines. (A–B) IHC and quantification in tumor vs. normal. (C–D) Protein levels. (E–G) OAS1 protein and GFP in transfected HeLa cells.(N.normal; T.tumor;)

10. OAS1 promotes HeLa cell migration, invasion, and upregulates reactive oxygen

species levels

To investigate the regulatory role of OAS1 in the malignant phenotype of cervical cancer cells, we performed functional experiments. Wound healing assays showed that OAS1 overexpression significantly enhanced the migration ability of HeLa cells, whereas knockdown inhibited cell migration (Figures 11A,-B). Transwell assays confirmed that OAS1 knockdown significantly suppressed the migration and invasion abilities of HeLa cells (Figures 11C-D), demonstrating that OAS1 positively regulates the invasive and metastatic capacity of cervical cancer cells.

ROS-mediated oxidative stress is involved in malignant tumor progression. ROS detection results showed that OAS1 knockdown reduced ROS levels in HeLa cells, whereas OAS1 overexpression significantly increased intracellular ROS levels and enhanced the oxidative stress response (Figures 11E-F). In conclusion, OAS1 can mediate malignant biological behaviors such as migration and invasion in cervical cancer cells by regulating oxidative stress levels.

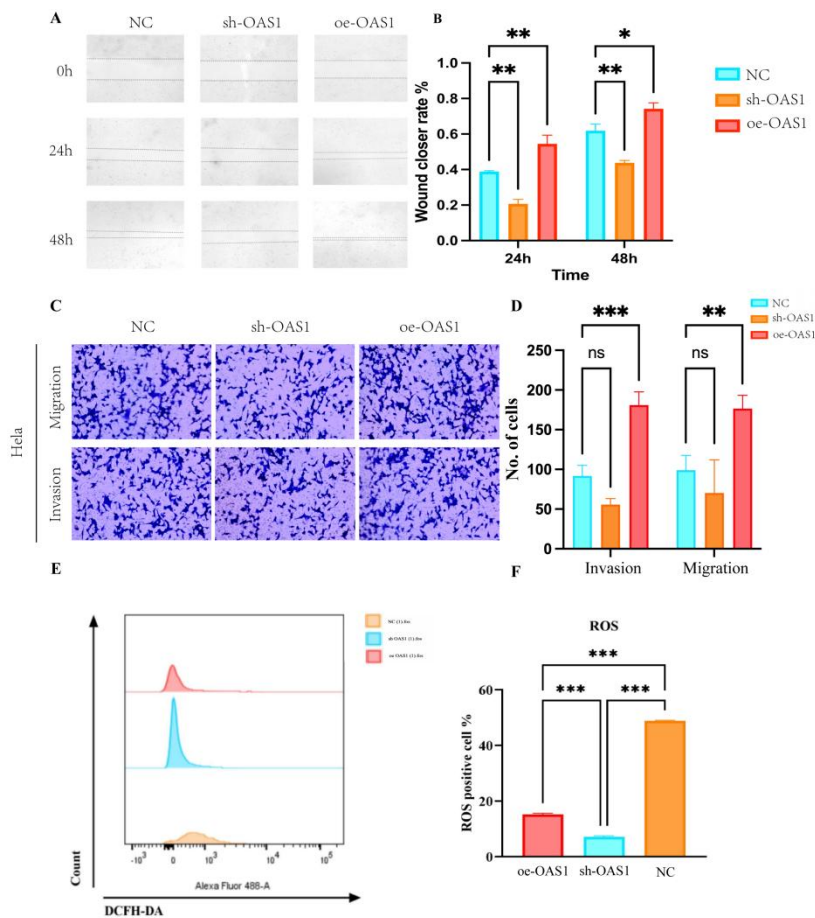


Figure 11. OAS1 promotes cell migration, invasion, and ROS generation in vitro.

(A–B) Wound-healing assay; (C–D) Transwell migration and invasion; (E–F) ROS detection by flow cytometry in HeLa cells with OAS1 knockdown or overexpression.

DISCUSSION

Cervical cancer is one of the most common gynecological malignancies. Although HPV vaccination and screening strategies have been continuously improved, high-risk HPV infection remains prevalent, and the incidence of cervical cancer has shown a trend toward younger age in recent years [21–22]. A considerable proportion of patients are still diagnosed at intermediate or advanced stages, and the prognosis of patients with recurrent or advanced disease remains unsatisfactory. In recent years, immunotherapy and targeted therapy have achieved certain advances; however, therapeutic efficacy varies markedly among individuals. Therefore, further elucidation of the molecular mechanisms underlying cervical cancer initiation and progression, as well as the identification of novel diagnostic, prognostic, and therapeutic targets, remains of great significance [23–24].

OAS1 is an important member of the 2'-5'-oligoadenylate synthetase family. The human OAS family mainly includes OAS1, OAS2, OAS3, and OASL. OAS1 is a typical interferon-inducible gene and one of the interferon-stimulated genes, playing a key role in innate immunity and antiviral responses. OAS1 can be induced by type I interferons and, upon recognition of viral double-stranded RNA, catalyzes ATP to generate 2'-5'-oligoadenylates. These molecules subsequently activate RNase L, promoting the degradation of viral RNA and partial cellular RNA, thereby inhibiting viral replication and enhancing host antiviral responses. In addition to its classical antiviral function, OAS1 may also participate in cellular growth, apoptosis, differentiation, and gene expression regulation [25]. Therefore, aberrant OAS1 expression may not only reflect activation of interferon signaling or antiviral immune status, but may also be associated with tumor cell proliferation, cell death, stress responses, and remodeling of the tumor immune microenvironment [26–27].

In this study, we systematically evaluated the expression characteristics, genetic alterations, prognostic value, cancer stemness, RNA modifications, immune infiltration, and immunotherapy-related significance of OAS1 across multiple cancer types based on multi-database pan-cancer analyses. We further explored its potential role in cervical cancer. The results showed that OAS1 was upregulated at both the mRNA and protein levels in multiple cancers, and its expression was closely associated with tumor stage, metastasis, genetic

alterations, poor prognosis, cancer stemness, RNA modification-related genes, and immune microenvironment features. HPA protein staining further supported the elevated expression trend of OAS1 in various tumor tissues. However, its expression patterns and prognostic implications were not completely consistent across different cancer types, suggesting that the biological role of OAS1 may be cancer type-dependent.

Clinical correlation analysis showed that OAS1 expression was associated with tumor stage, distant metastasis, and lymph node metastasis in certain cancers, suggesting its potential value as a disease progression-related biomarker. Genetic alteration analysis revealed that OAS1 exhibited mutations, amplifications, deletions, and copy number variations in multiple cancers. Missense mutations were the predominant mutation type, and some mutation sites were located within the OAS1_C functional domain. In addition, increased OAS1 copy number was associated with elevated mRNA expression, indicating that genomic alterations may represent one of the important mechanisms underlying OAS1 dysregulation. Prognostic analysis showed that high OAS1 expression was associated with poorer survival in GBMLGG, LGG, PAAD, ACC, LUAD, LIHC, and UVM, whereas in BLCA, SKCM, MESO, and ALL, high OAS1 expression appeared to be associated with a lower risk of death. These findings indicate that the prognostic value of OAS1 should be interpreted in the context of specific cancer types, molecular subtypes, and immune backgrounds.

Functional enrichment analysis demonstrated that OAS1 and its co-expressed genes were mainly enriched in immune-related processes, including type I interferon signaling, antiviral response, innate immune response, cytokine-mediated signaling, the NOD-like receptor signaling pathway, and the RIG-I-like receptor signaling pathway. Co-expressed genes such as OAS2, OAS3, ISG15, IFI44, and IFI6 were closely related to interferon responses or antiviral immunity, suggesting that OAS1 may function within a co-expression network centered on interferon signaling and innate immune activation. Immune infiltration analysis further showed that OAS1 was associated with ImmuneScore, StromalScore, ESTIMATEScore, and the infiltration levels of multiple immune cell types. In particular, OAS1 expression was correlated with the infiltration of B cells, CD4⁺ T cells, CD8⁺ T cells, macrophages, dendritic cells, and neutrophils. Meanwhile, OAS1 was also associated with TMB, MSI, and immune checkpoint-related molecules such as PDCD1, CTLA4, and TIGIT, suggesting that OAS1 may reflect a tumor microenvironment characterized by concurrent immune activation and immune suppression.

In cervical cancer, IHC and Western blotting further confirmed that OAS1 was highly

expressed in tumor tissues. In vitro experiments showed that OAS1 overexpression promoted the migration of HeLa cells and increased ROS levels, whereas OAS1 knockdown suppressed migration- and invasion-related phenotypes and reduced ROS levels. These findings suggest that OAS1 may participate in the malignant progression of cervical cancer by regulating oxidative stress. Single-cell transcriptomic analysis further revealed that OAS1 was highly expressed not only in epithelial/tumor cells but also enriched in monocyte/macrophage populations. This suggests that OAS1 may be involved in both tumor cell-intrinsic malignant behavior and immune microenvironment regulation, serving as an important molecule linking tumor cell migration and invasion, oxidative stress, and immune cell state alterations.

This study has several limitations. First, the pan-cancer analysis was mainly based on public databases, and the results were primarily correlative. Second, the sample size for clinical validation in cervical cancer was limited, and the in vitro functional experiments were mainly performed in HeLa cells; therefore, further validation in larger clinical cohorts, additional cervical cancer cell lines, and in vivo models is needed. Finally, the precise mechanisms by which OAS1 regulates ROS levels and the immune microenvironment remain to be clarified through rescue experiments, ROS scavenger intervention, transcriptome sequencing, and pathway inhibition assays. In summary, OAS1 may serve as a potential diagnostic, prognostic, and immune microenvironment-related biomarker in multiple cancers. In cervical cancer, OAS1 may contribute to tumor progression by enhancing cell migration, invasion, and oxidative stress, providing a theoretical basis for its potential role as a therapeutic target.

Supplementary Materials

Table S1. Abbreviations for Cancers

Abbreviation	Name
ACC	Adrenocortical carcinoma
ALL	Acute Lymphoblastic Leukemia
BLCA	Bladder Urothelial Carcinoma
BRCA	Breast invasive carcinoma
CESC	Cervical squamous cell carcinoma and endocervical adenocarcinoma
CHOL	Cholangiocarcinoma
COAD	Colon adenocarcinoma
COADREAD	Colon adenocarcinoma/Rectum adenocarcinoma
DLBC	Lymphoid Neoplasm Diffuse Large B-cell Lymphoma
ESCA	Esophageal carcinoma
GBM	Glioblastoma multiforme
GBMLGG	Glioma

HNSC	Head and Neck squamous cell carcinoma
KICH	Kidney Chromophobe
KIPAN	Pan-kidney cohort (KICH + KIRC + KIRP)
KIRC	Kidney renal clear cell carcinoma
KIRP	Kidney renal papillary cell carcinoma
LAML	Acute Myeloid Leukemia
LGG	Brain Lower Grade Glioma
LIHC	Liver hepatocellular carcinoma
LUAD	Lung adenocarcinoma
LUSC	Lung squamous cell carcinoma
MESO	Mesothelioma
NB	Neuroblastoma
OV	Ovarian serous cystadenocarcinoma
PAAD	Pancreatic adenocarcinoma
PCPG	Pheochromocytoma and Paraganglioma
PRAD	Prostate adenocarcinoma
READ	Rectum adenocarcinoma
SARC	Sarcoma
SKCM	Skin Cutaneous Melanoma
SKCM-M	Metastatic Skin Cutaneous Melanoma
SKCM-P	Primary Skin Cutaneous Melanoma
STAD	Stomach adenocarcinoma
STES	Stomach and Esophageal carcinoma
TGCT	Testicular Germ Cell Tumors
THCA	Thyroid carcinoma
THYM	Thymoma
UCEC	Uterine Corpus Endometrial Carcinoma
UCS	Uterine Carcinosarcoma
UVM	Uveal Melanoma

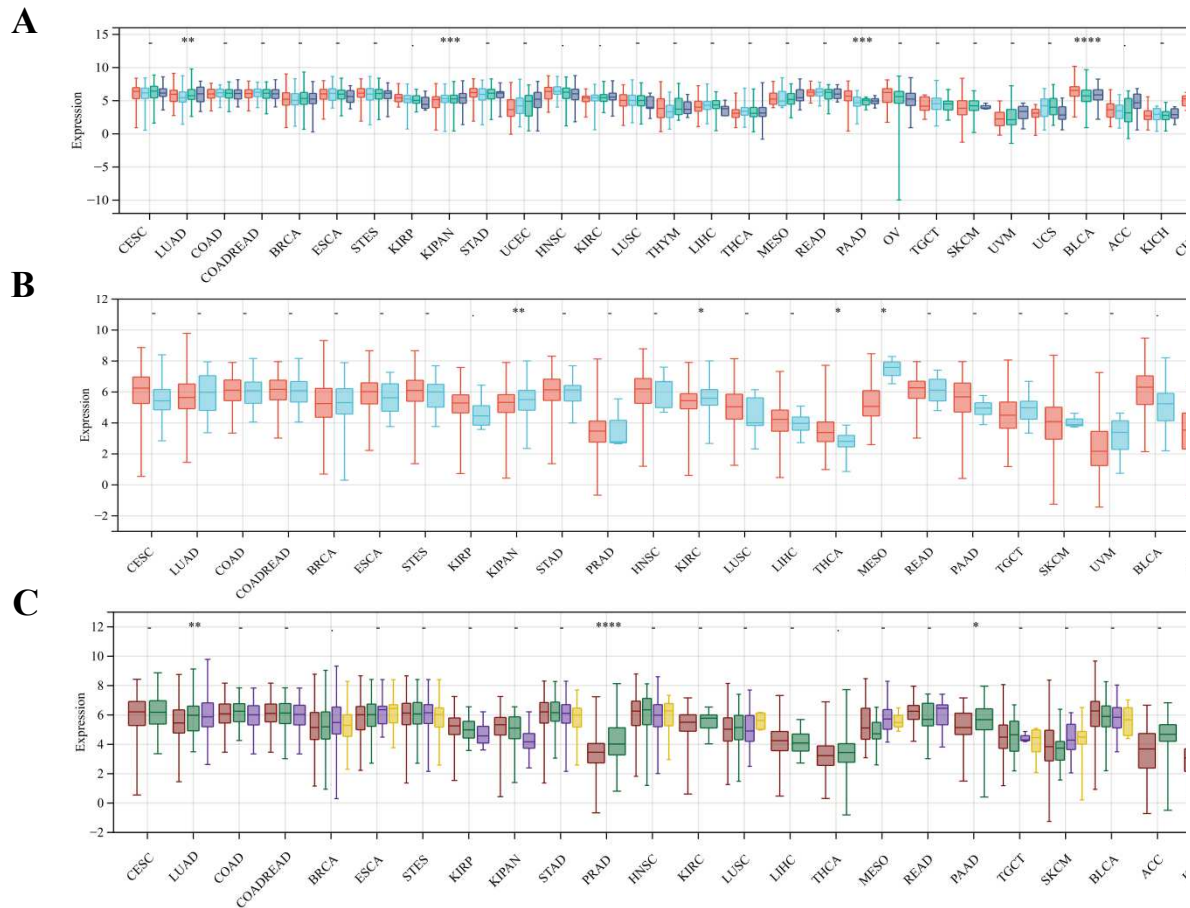


Figure S1. Expression Analysis of OAS1 Across Multiple Cancers According to Tumor Stage, Metastasis Status, and Lymph Node Infiltration

(A) Boxplots showing OAS1 expression levels in different cancers stratified by tumor stage (I–V). Each box represents the median and distribution of OAS1 expression within a specific stage for each cancer type.

(B) Boxplots depicting the association between OAS1 expression and metastasis status (M0 vs. M1) across multiple cancers. M0 (no distant metastasis) is shown in red, and M1 (presence of distant metastasis) is shown in blue.

(C) Boxplots illustrating OAS1 expression levels in multiple cancers according to lymph node infiltration (N0–N3).

All analyses were based on data obtained from the SangerBox database. Statistical significance of OAS1 expression differences is indicated by asterisks.

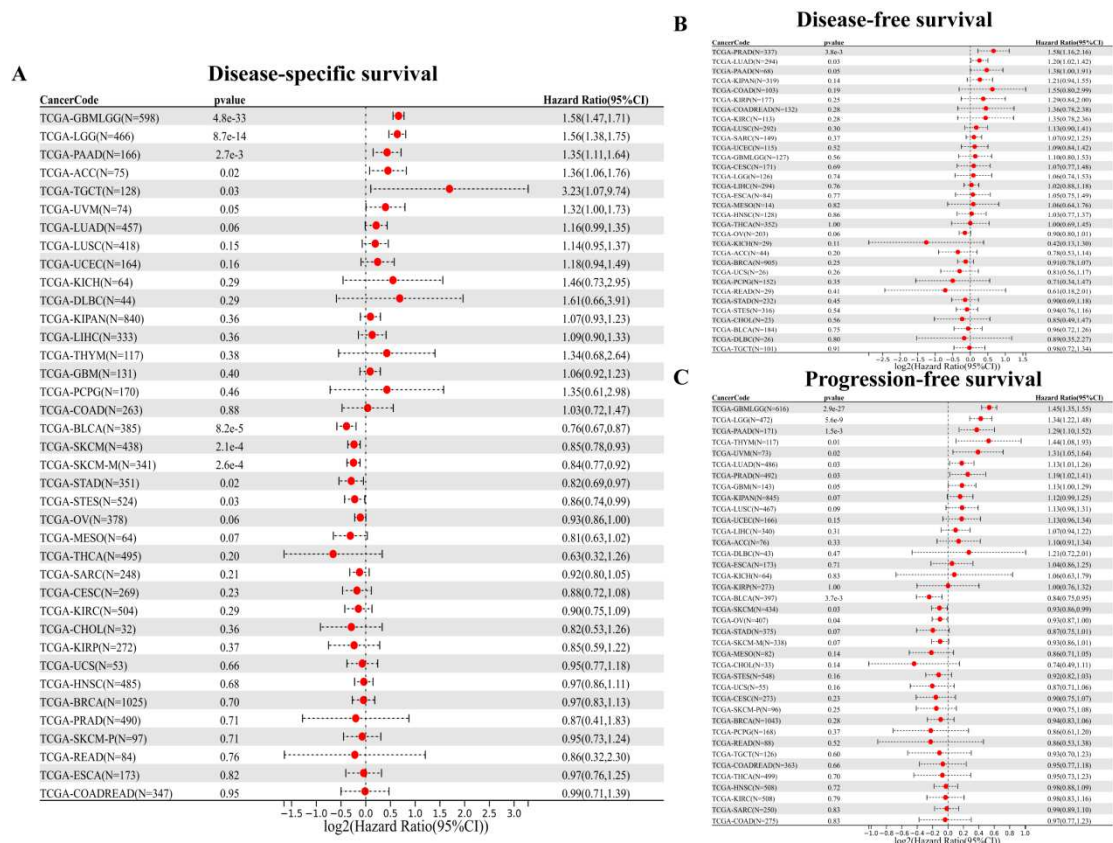


Figure S2. Correlation Analysis Between OAS1 Expression and Survival Prognosis Across Different Cancers

(A) Forest plot showing the association between OAS1 expression and disease-specific survival (DSS) in multiple cancers. Hazard ratios (HRs) and 95% confidence intervals (CIs) are presented. An HR > 1 indicates that high OAS1 expression is associated with poorer patient survival. (B) Forest plot depicting the correlation between OAS1 expression and disease-free survival (DFS), showing log₂-transformed HRs [Log₂(HR)] and 95% CIs for each cancer type. (C) Forest plot illustrating the association between OAS1 expression and progression-free survival (PFS), with corresponding log₂-transformed HRs [Log₂(HR)] indicated. All analyses were conducted using the SangerBox online platform.

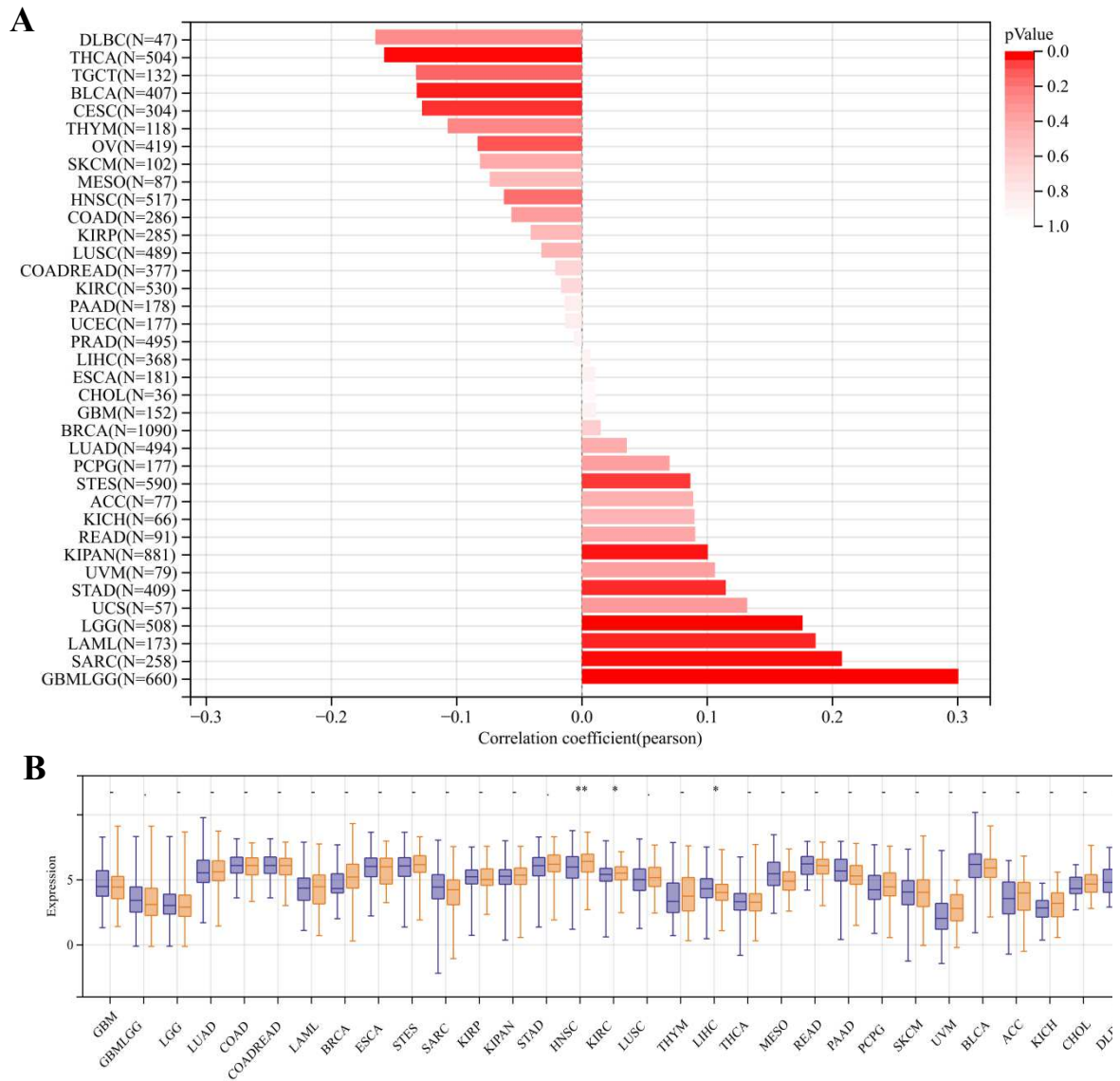


Figure S3. Correlation Analysis Between OAS1 Expression and Patient Age or Sex Across Multiple Cancers

(A) Bar plots showing Pearson correlation coefficients between OAS1 expression and patient age across various cancers. Each bar represents the strength of the correlation, with red color shades indicating different p-values (darker colors correspond to more statistically significant differences). (B) Boxplots comparing OAS1 expression levels between male and female patients across multiple cancers. Blue-gray boxes represent male patients, and light orange boxes represent female patients. Statistical significance of sex-based differences is indicated by asterisks (* $P < 0.05$). Each box displays the median OAS1 expression and distribution for the corresponding cancer type.

397 **Conflict of Interest**

398 No potential conflict of interest relevant to this article was reported.

399 **Data Availability**

400 The corresponding author will respond to reasonable requests for the datasets used in the current work.

401 **Author Contributions**

402 YW: Writing – original draft.JN: Resources, Writing – review & editing.YL: Data curation, Formal analysis.

403 XW: Data curation, Methodology. QL: Data curation. SH: Formal analysis, Supervision. JW: Software,

404 Supervision.

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REFERENCES

1. Roerden M, Spranger S. Cancer immune evasion, immunoediting and intratumour heterogeneity. *Nat Rev Immunol.* 2025;25(5):353-369.
2. Feng K, Zhang X, Li J, Han M, Wang J, Chen F, et al. Neoantigens combined with in situ cancer vaccination induce personalized immunity and reshape the tumor microenvironment. *Nat Commun. Nat Commun.* 2025;16(1):5074.
3. Yi M, Niu M, Xu L, Luo S, Wu K. Regulation of PD-L1 expression in the tumor microenvironment. *J Hematol Oncol.* 2021;14(1):10.
4. Pessoa LS, Heringer M, Ferrer VP. ctDNA as a cancer biomarker: A broad overview. *Crit Rev Oncol Hematol.* 2020;155:103109.
5. Hammarström S. The carcinoembryonic antigen (CEA) family: structures, suggested functions and expression in normal and malignant tissues. *Semin Cancer Biol.* 1999;9(2):67-81.
6. Höti N, Lih TS, Dong M, Zhang Z, Mangold L, Partin AW, et al. Urinary PSA and Serum PSA for Aggressive Prostate Cancer Detection. *Cancers (Basel).* 2023;15(3):960.
7. Huai W, Yang K, Xing C, Song K, Lyu H, Williams NS, et al. OAS cross-activates RNase L intercellularly through cell-to-cell transfer of 2-5A to spread innate immunity. *Immunity.* 2025;58(4):797-810.e6.
8. Yang K, Dong B, Asthana A, Silverman RH, Yan N. RNA helicase SKIV2L limits antiviral defense and autoinflammation elicited by the OAS-RNase L pathway. *EMBO J.* 2024;43(18):3876-3894.
9. Lee D, Malathi K, Okano T, Nakajima K, Cobat A, Morio T, et al. The OAS-RNase L pathway: Insights from experiments of nature. *Sci Immunol.* 2026;11(115):eads9407.
10. Di H, Elbahesh H, Brinton MA. Characteristics of Human OAS1 Isoform Proteins. *Viruses.* 2020;12(2):152.
11. Harioudh MK, Perez J, Chong Z, Nair S, So L, McCormick KD, et al. Oligoadenylate synthetase 1 displays dual antiviral mechanisms in driving translational shutdown and protecting interferon production. *Immunity.* 2024;57(3):446-461.e7.
12. Le Pen J, Rice CM. The antiviral state of the cell: lessons from SARS-CoV-2. *Curr Opin Immunol.* 2024;87:102426.
13. Aalegría-Carrasco E, Jaén-Castaño M, Delgado-Wicke P, Zurita-Cruz ND, Montes N, Roy-Vallejo E, et al. Modulation of TLR7, TYK2 and OAS1 expression during SARS-CoV-2 infection. *Front Immunol.* 2025;16:1713928.
14. Zhang Y, Yu C. Prognostic characterization of OAS1/OAS2/OAS3/OASL in breast cancer. *BMC Cancer.* 2020;20(1):575.
15. Lu L, Wang H, Fang J, Zheng J, Liu B, Xia L, et al. Overexpression of OAS1 Is Correlated With Poor Prognosis in Pancreatic Cancer. *Front Oncol.* 2022;12:944194.
16. Lai Y, Wang X, Ma J, Du C, Wang Y, Wang Y, et al. Knockdown of EIF2AK2-OAS1 axis reduces ATP production inducing AMPK phosphorylation to inhibit the malignant behavior of gastric cancer cells. *J Bioenerg Biomembr.* 2024;56(4):433-449.
17. Jiang S, Deng X, Luo M, Zhou L, Chai J, Tian C, et al. Pan-cancer analysis identified OAS1 as a potential prognostic biomarker for multiple tumor types. *Front Oncol.* 2023;13:1207081.
18. Wang L, Gao L, Ding F, Gao K, Liu Q, Yin X. Prognostic value and molecular mechanisms of OAS1 in lung adenocarcinoma. *BMC Pulm Med.* 2024;24(1):473.
19. Kanehisa M, Furumichi M, Sato Y, Matsuura Y, Ishiguro-Watanabe M. KEGG: biological systems database as a model of the real world. *Nucleic Acids Res.* 2025;53(D1):D672-D677.
20. Kanehisa M. Toward understanding the origin and evolution of cellular organisms. *Protein Sci.* 2019;28(11):1947-1951.
21. Ni H, Huang C, Ran Z, Li S, Kuang C, Zhang Y, et al. Targeting HPV for the prevention, diagnosis, and treatment of cervical cancer. *J Mol Cell Biol.* 2025;16(10):mjae046.
22. Wang R, Pan W, Jin L, Huang W, Li Y, Wu D, et al. Human papillomavirus vaccine against cervical cancer: Opportunity and challenge. *Cancer Lett.* 2020;471:88-102.
23. Duska LR, Podwika SE, Randall LM. Top advances of the year: Cervical cancer. *Cancer.* 2024;130(15):2571-2576.
24. Verhoeven Y, Quatannens D, van der Heijden S, Claes J, de Beukelaar J, Lambrechts H, et al. CD155 links tumor immunotype to epithelial-directed precision therapy beyond checkpoint inhibition in cervical cancer. *J Immunother Cancer.* 2026;14(5):e014834.
25. Gao LJ, He ZM, Li YY, Yang RR, Yan M, Shang X, et al. Role of OAS gene family in COVID-19 induced heart failure. *J Transl Med.* 2023;21(1):212.
26. Che L, Yang H, Wang D, Liu S. Corylin sensitizes breast cancer cells to overcome tamoxifen resistance by

467 regulating OAS1/miR-22-3p/SIRT1 axis. *Acta Biochim Pol.* 2021;68(4):757-764.
468 27. Lu D, Di S, Zhuo S, Zhou L, Bai R, Ma T, et al. The long noncoding RNA TINCR promotes breast cancer cell
469 proliferation and migration by regulating OAS1. *Cell Death Discov.* 2021;7(1):41.
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