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ORIGINAL RESEARCH

ITGA11, a Prognostic Factor Associated with Immunity in Gastric Adenocarcinoma

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Background: Stomach adenocarcinoma (STAD) presents a challenge given its advanced stage at diagnosis and poor prognosis. Integrin subunit alpha 11 (ITGA11) encodes alpha integrin and has been implicated in promoting tumorigenesis and development by participating in cell proliferation and invasion. However, the precise mechanism of ITGA11 in STAD remains unclear.

Methods: The differences in ITGA11 expression levels between 375 gastric cancer samples and 32 paracancerous tissue samples from the Cancer Genome Atlas (TCGA) database were examined. The relationship between ITGA11 expression and clinical features and ITGA11 diagnostic and prognostic value were evaluated using the chi-square test and receiver operating characteristic (ROC) assay. Differentially expressed genes were identified based on ITGA11 expression. Subsequently, functional enrichment analyses were conducted using Gene Ontology, the Kyoto Encyclopedia of Genes and Genomes, and Gene Set Enrichment Analysis. Furthermore, immune infiltration and the expression of ITGA11-associated immune checkpoints in patients with tumors were assessed using CIBERSORT, single-sample gene set enrichment analysis, and the TIMER database. Drug sensitivity associated with ITGA11 expression was analyzed using the R oncoPredict package to guide treatment decisions. Finally, the difference in ITGA11 expression between cancer tissue and the adjacent tissues was validated using quantitative PCR (qPCR) and immunohistochemistry.

Results: The gastric cancer tissue had significantly upregulated ITGA11 expression compared to paracancerous tissues. ITGA11 demonstrated robust diagnostic and prognostic value in gastric cancer (GC) and was an independent risk factor for adverse outcomes. The patients with STAD with elevated ITGA11 expression levels had heightened immune cell infiltration and increased immune checkpoint marker expression. Notably, patients with increased ITGA11 expression demonstrated reduced responsiveness to oxaliplatin and afatinib.

Conclusion: The results indicated the pivotal role of ITGA11 in shaping the tumor immune microenvironment, ultimately establishing ITGA11 as an immune-related prognostic predictor within the intricate landscape of STAD.

Keywords: ITGA11, stomach adenocarcinoma, bioinformatics analysis, immune infiltration, prognosis

Introduction

Stomach adenocarcinoma (STAD) is the fifth most frequently diagnosed cancer and is the third leading cause of cancer-related mortality worldwide.[1] STAD is frequently clinically diagnosed at an advanced stage, resulting in high mortality rates and a substantial global burden.[2] By 2040, the number of new gastric cancer cases will rise to 1.77 million globally.[3] The overall survival of STAD has been improved by combination therapies involving chemotherapy, immunotherapy, or targeted therapy driven by advances in molecular pathologies and the identification of therapeutic targets, such as HER2, FGFR2b, and CLDN18.2.[4] However, for both targeted therapies and immunotherapies, there is currently a lack of biomarkers that can accurately predict who will benefit best.[5] Therefore, there is a pressing need to explore the biomarkers related to gastric cancer tumorigenesis and development.

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Integrins are formed by the combination of α and β subunits, which are involved in constructing the extracellular matrix and intracellular cytoskeleton and are used in the main pathway for the binding and response of various protein ligands inside and outside the cell. The integrin family member integrin subunit alpha 11 (ITGA11) is upregulated in various tumors, including lung cancer, breast cancer, cutaneous squamous cell carcinoma, and esophageal cancer. ITGA11 influences prognosis by promoting cancer-associated fibroblast (CAF) migration.[6–14] Furthermore, ITGA11 is critical in myofibroblast differentiation, matrix reorganization, and collagen deposition.[15,16] ITGA11 is overexpressed in CAFs, contributing to tumor matrix construction and affecting the overall survival of patients with head and neck squamous cell carcinoma.[17] CAFs demonstrated enhanced tumor cell invasion activity in gastric cancer and mobilized immune cells to build the tumor immune microenvironment.[18,19] These previous studies collectively underscored the potential function of ITGA11 in tumorigenesis, suggesting its capability to drive malignant progression in various cancers. Moreover, ITGA11 possibly has an equally indispensable role in STAD. Previous studies indicated that ITGA11 expression was related to STAD prognoses, although the specific mechanism has not been systematically investigated.[20,21]

In the present study, ITGA11 differential expression in gastric cancer and adjacent normal tissues in the Cancer Genome Atlas (TCGA) database was investigated and verified using the Gene Expression Omnibus (GEO) dataset. The differentially expressed genes (DEGs) underwent functional enrichment analysis using R to explore the pathways related to ITGA11 immune infiltration function, study the relationship between its immune checkpoints, and predict drug sensitivity. ITGA11 expression in gastric cancer tissues and the adjacent tissues was verified using real-time quantitative PCR (RT-qPCR) and immunohistochemical methods.

Materials and Methods

Data Acquisition

Transcriptional RNA sequencing (RNA-seq) data were obtained from the Genomic Data Commons (GDC) Data Portal (https://gdc.xenahubs.net). The clinical information of 32 normal samples and 375 tumor samples were from TCGA. The GEO datasets GSE54129 and GSE15459 were utilized for verification.

ITGA11 Expression in STAD

The differences in ITGA11 expression between TCGA gastric cancer tissue and adjacent noncancerous tissue were analyzed using R (https://www.r-project.org/) and the edgeR package. ITGA11 expression difference was validated using the GSE54129 dataset.

Diagnosis and Prognostic Analysis

TCGA tumor samples were divided into two groups for survival analysis based on the ITGA11 expression (cut-off value: 50%). The survival curve was drawn using the R survival and survminer packages, while prognosis and diagnosis curves were constructed using timeroc and pROC. $P < 0.05$ was defined as a statistically significant difference. The difference between the groups was validated using GSE15459 dataset in Kaplan-Meier plotter (http://kmplot.com/analysis/).

Functional Enrichment Analysis

The DEGs combined with ITGA11 expression in TCGA tumor samples were selected using the R limma package. Differential expression was indicated by an adjusted p-value < 0.05 and Ilog2 fold change (FC)I ≥ 1. The enrichment analysis was explored using the R packages clusterProfiler and Enrichment plot and using Gene Ontology (GO) functional enrichment, the Kyoto Encyclopedia of Genes and Genomes (KEGG), and gene set enrichment analysis (GSEA).

Immune Infiltration

The proportion of tumor-infiltrating immune cells was estimated by CIBERSORT based on the gene expression profiles of all STAD samples. The infiltration degree of 28 immune cell types was quantified using the R package GSVA utilizing single-sample GSEA (ssGSEA). The correlation between ITGA11 expression and immune cells was investigated in the TIMER database (https://cistrome.shinyapps.io/timer/).

Immune Checkpoint Correlation Analysis

The correlation between ITGA11 and immune checkpoints was examined using the Spearman correlation. The correlation between ITGA11 expression and immune checkpoints was validated using the TIMER database (https://cistrome.shinyapps.io/timer/).

Protein–Protein Interaction Network

The STRING database generated a Protein–protein interaction (PPI) network of DEGs with high confidence (0.400) and medium false discovery rate (FDR) stringency (5%). Cytoscape software was used for further analysis, where the top 10 hub genes with synergy with ITGA11 were identified with the cytoHubba plugin. Cox regression analysis and survival analysis of the hub genes were conducted using the R survival package and visualized using the R packages forest plot, survival, and survminer (cut-off value: 50%).

Antineoplastic Drug Sensitivity

The drug sensitivity of TCGA samples was analyzed using the R package oncoPredict. The relationship between the median inhibitory concentration (IC_{50}) of the drugs and ITGA11 expression was then analyzed using the Wilcoxon test (cut-off value: 50%).

Quantitative Real-Time PCR

Cancer and para-cancer tissues were obtained from 31 patients at the First Affiliated Hospital of Guangxi Medical University. The specimens were acquired in compliance with the Declaration of Helsinki and with all participants' explicit consent and written approval. The First Affiliated Hospital of Guangxi Medical University Medical Ethics Committee approved the research protocol and procedure for acquiring human samples (approval number: 2023-E461-01). Total RNA was extracted from the specimens and then reverse-transcribed to complementary DNA (cDNA). ITGA11 expression was quantitatively analyzed using quantitative real-time (qRT) PCR using SYBR Green Premix (YEASEN, China). The internal reference was β-actin. The *ITGA11* primer sequences were as follows: 5′-GGAGGAAGACTTGCGTCG-3′ (forward) and 5′-CACAGGTTCCCCAGTAGATG-3′ (reverse). The relative mRNA expression was quantified by the comparative threshold cycle ($2^{-\Delta\Delta Ct}$) method.

Immunohistochemistry

ITGA11 protein expression was assessed using immunohistochemical analysis of 50 gastric cancer cases and 40 adjacent tissues. Immunohistochemistry (IHC) was conducted as follows: after deparaffinization, rehydration, and antigen retrieval, tissue sections were incubated overnight with anti-ITGA11 antibody (1:100 dilution, Elabscience, China) at 4 °C. Following secondary antibody incubation, the sections were stained sequentially with 3,3′-diaminobenzidine (DAB) and hematoxylin. The sections were analyzed using an optical microscope. ITGA11 expression levels were quantified using the average optical density (AOD).

Results

ITGA11 Expression in Tumors and Its Diagnostic and Prognostic Significance in STAD

The gastric cancer tissues had significantly higher ITGA11 expression levels (n = 375) compared to normal tissues (n = 32) (Figure 1A). The receiver operating characteristic (ROC) curve analysis yielded an area under the curve (AUC) value of 0.822 with a 95% confidence interval (95% CI) of 0.763–0.881, indicating its effectiveness in

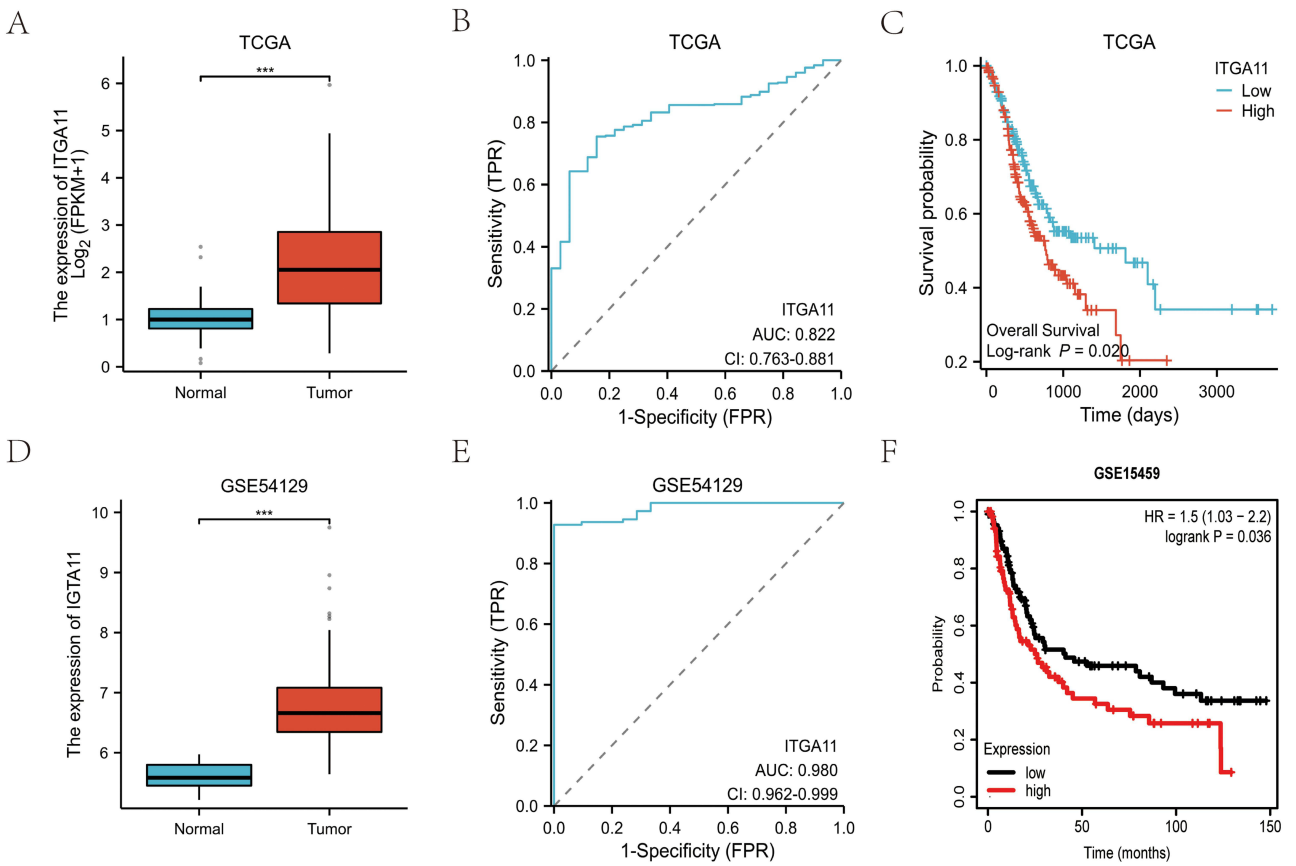

Figure 1 Difference in ITGA11 expression between gastric cancer and normal tissues, and its diagnostic and prognostic value in STAD. (**A**) ITGA11 was overexpressed in STAD compared to normal groups in TCGA dataset. (**B**) Diagnostic ROC curve of ITGA11 in TCGA dataset. (**C**) Kaplan–Meier curve of ITGA11 in TCGA dataset. (**D**) Differential expression of ITGA11 in STAD and normal groups in GSE54129. (**E**) Diagnostic ROC curve of ITGA11 in GSE54129. (**F**) Kaplan–Meier curve of ITGA11 in GSE15459. ***p < 0.001.

Abbreviations: ITGA11, Integrin subunit alpha 11; STAD, stomach adenocarcinoma; TCGA, The Cancer Genome Atlas; FPKM, fragments per kilobase of transcript per million reads mapped; ROC, receiver operator characteristic; AUC, area under the curve; TPR, true positive rate; FPR, false positive rate; CI, confidence interval; GEO, Gene Expression Omnibus; HR, hazard ratio.

distinguishing normal tissue from gastric adenocarcinoma tissue (Figure 1B). The Kaplan–Meier curve analysis revealed that patients with gastric cancer with elevated ITGA11 expression had shorter overall survival than those with lower ITGA11 expression (p = 0.020) (Figure 1C).

Concurrently, a complementary analysis was conducted using the GEO database (GSE54129 and GSE15459). In GSE54129, ITGA11 expression in gastric cancer tissues significantly exceeded that in normal tissues (Figure 1D), and diagnostic ROC curve analysis confirmed its robust diagnostic efficacy (AUC = 0.980, 95% CI = 0.962–0.999) (Figure 1E). Subsequently, the GSE15459 dataset validated the association between high ITGA11 expression and lower survival rates in patients with gastric cancer (p = 0.036) (Figure 1F).

Correlation Between ITGA11 Expression and Clinical Features

Analysis of the correlation between ITGA11 and clinical features in STAD yielded notable associations with local progression and prognosis. The ITGA11 clinical prognostic value in GC was assessed using univariate and multivariate Cox regression analyses. The univariate analysis identified ITGA11 (hazard ratio [HR] = 1.483, p = 0.02), age (HR = 1.620, p = 0.005), T stage (HR = 8.829, p < 0.001), N stage (HR = 1.925, p = 0.001), M stage (HR = 2.254, p = 0.01), and clinical stage (HR = 2.247, p = 0.004) as significant factors for overall survival in STAD (Figure 2A). The multivariate analysis confirmed that ITGA11 (HR = 1.614, p = 0.009), age (HR = 1.810, p = 0.002), and M stage (HR = 2.398, p = 0.005) were independent prognostic factors for STAD (Figure 2B). Interestingly, ITGA11 expression was increased in

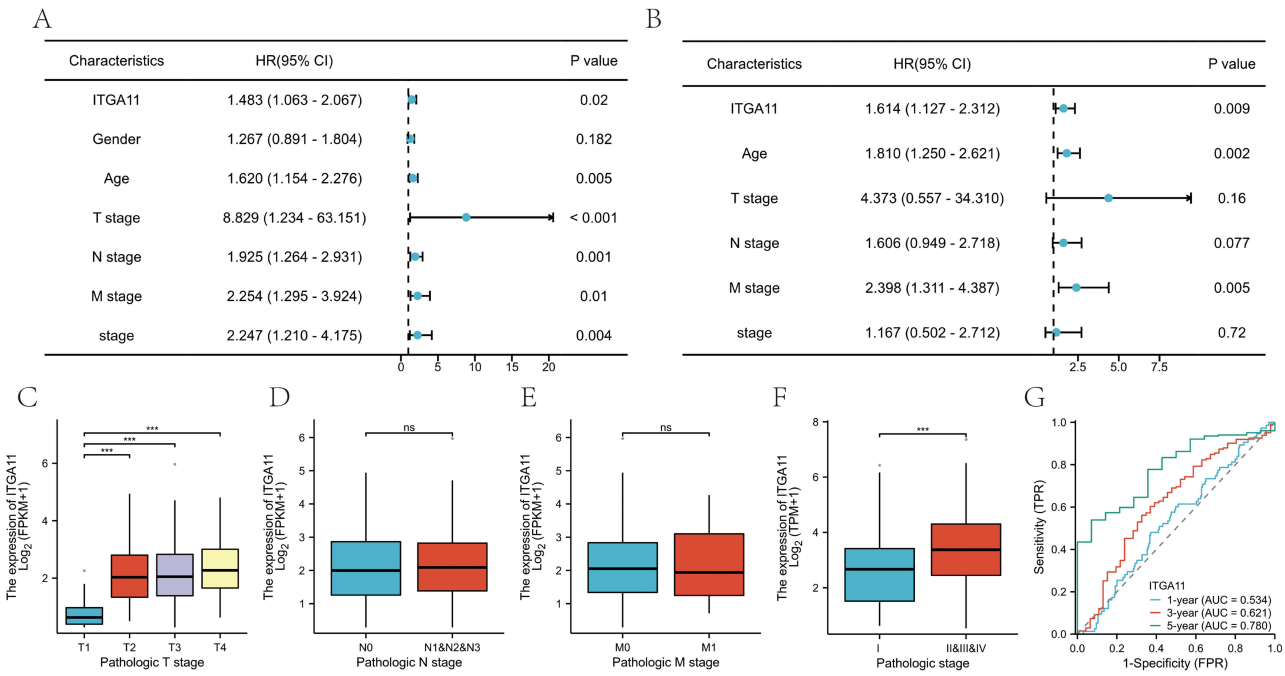

Figure 2 ITGA11 is an independent risk factor for adverse outcomes in STAD and its relationship with clinical characteristics. (**A**) Univariate Cox regression analysis. (**B**) Multivariate Cox regression analysis. (**C**) Comparison of ITGA11 expression according to T stage. (**D**) Comparison of ITGA11 expression according to N stage. (**E**) Comparison of ITGA11 expression according to M stage. (**F**) Comparison of ITGA11 expression according to pathological stage. (**G**) One-, three-, and five-year ROC curve analyses of ITGA11. ***p < 0.001.

Abbreviations: ns, no significance; ITGA11, Integrin subunit alpha 11; STAD, stomach adenocarcinoma; HR, hazard ratio; FPKM, fragments per kilobase of transcript per million reads mapped; AUC, area under the curve; TPR, true positive rate; FPR, false positive rate.

high pathologic T stages and advanced stages in patients with STAD (Figure 2C and F) but demonstrated no significant differences for the N and M stages (Figure 2D and E). The one-, three-, and five-year ITGA11 prognostic AUC values were 0.534 (95% CI = 0.461–0.6071), 0.621 (95% CI = 0.5241–0.7188), and 0.780 (95% CI = 0.6746–0.8846), respectively (Figure 2G).

Functional Predictions of ITGA11 Related to Immune Activity

In TCGA-STAD, the comparison of two ITGA11 expression groups identified 1053 DEGs (377 upregulated genes and 676 downregulated genes) (Figure 3A). GSEA revealed associations between the DEGs and immune-related processes and tumorigenesis, including pathways such as WP_PI3KAKT_SIGNALING_PATHWAY, KEGG_PATHWAYS_IN_CANCER, PID_P53_DOWNSTREAM_PATHWAY, REACTOME_INNATE_IMMUNE_SYSTEM, and REACTOME_DISEASES_OF_METABOLISM (Figure 3B).

The GO/KEGG enrichment analysis revealed that the DEGs were notably enriched in immune-related activities involving pathways such as that for humoral immune response, negative regulation of immune system process, phagocytosis, engulfment, B cell-mediated immunity, egulation of leukocyte migration, immunoglobulin-mediated immune response, positive regulation of B cell activation, B cell receptor signaling pathway, humoral immune response mediated by circulating immunoglobulin, negative regulation of leukocyte differentiation, regulation of extrinsic apoptotic signaling pathway via death domain receptors, Golgi lumen, immunoglobulin complex, cytokine binding, immunoglobulin receptor binding, oxygen binding, alcohol dehydrogenase (NADP+) activity, PI3K–Akt signaling, drug metabolism: cytochrome P450, and chemical carcinogenesis: DNA adducts (Figure 3C and D).

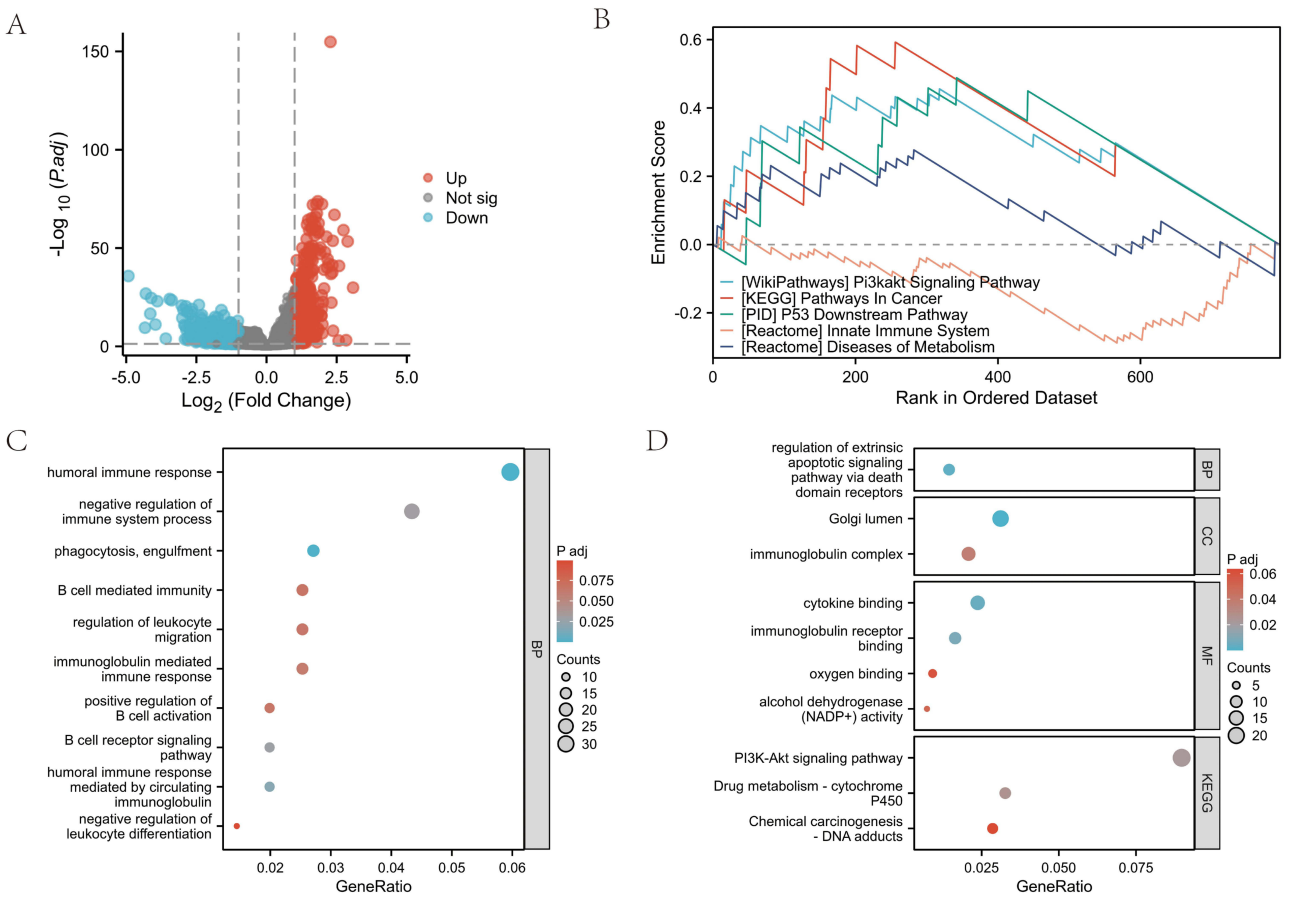

Figure 3 Functional analysis of DEGs. (**A**) Volcano map of the significant DEGs identified based on ITGA11 expression in STAD. (**B**) GSEA of the DEGs. (**C**) GO enrichment in the biological process (BP) of DEGs. (**D**) GO enrichment in biological process (BP), cell composition (CC), molecular function (MF), and KEGG enrichment of DGEs.
Abbreviations: DEGs, Differential expression genes; ITGA11, integrin subunit alpha 11; STAD, stomach adenocarcinoma; GSEA, gene set enrichment analysis; PID, Pathway Interaction Database; GO, Gene Ontology; KEGG, Kyoto Encyclopedia of Genes and Genomes.

The Relationship Between ITGA11 and Immune Infiltration

The proportion of immune subsets infiltrating in STAD was analyzed using the CIBERSORT algorithm to investigate the connection between ITGA11 expression and the immune microenvironment (Figure 4A). The high ITGA11 expression group exhibited higher ESTIMATE, immune, and stromal scores (Figure 4B). Furthermore, the ssGSEA algorithm demonstrated increased expression of multiple immune subsets in the high-expression group, encompassing CD8 active T cells, cytotoxic cells, dendritic cells, eosinophils, macrophages, mast cells, neutrophils, natural killer (NK) cells, T cells, effective memory T cells, T follicular helper cells, and Th1 cells (Figure 4C). Additionally, correlation analyses indicated a positive correlation between ITGA11 expression and CD8 active T cells, CD4 active T cells, macrophages, neutrophils, and dendritic cells, and an inverse correlation with memory B cells (Figure 4D).

Expression of ITGA11-Related Immune Checkpoints

Spearman correlation analysis conducted to elucidate the mechanism of ITGA11 influence on the immune microenvironment revealed significant positive correlations between ITGA11 expression and common immune checkpoints (PDCD1, CD274, PDCD1LG2, CTLA4, HAVCR2, LILRB1, SIRPA, LAG3, CD8A, and TIGIT) (Figure 5A–K).

PPI Network Construction and Hub Gene Selection

A PPI network was constructed using STRING and Cytoscape to elucidate interactions between ITGA11 and binding proteins. The top 10 hub genes were identified and formed a PPI network that included *BGN, MMP2, LOX, POSTN,*

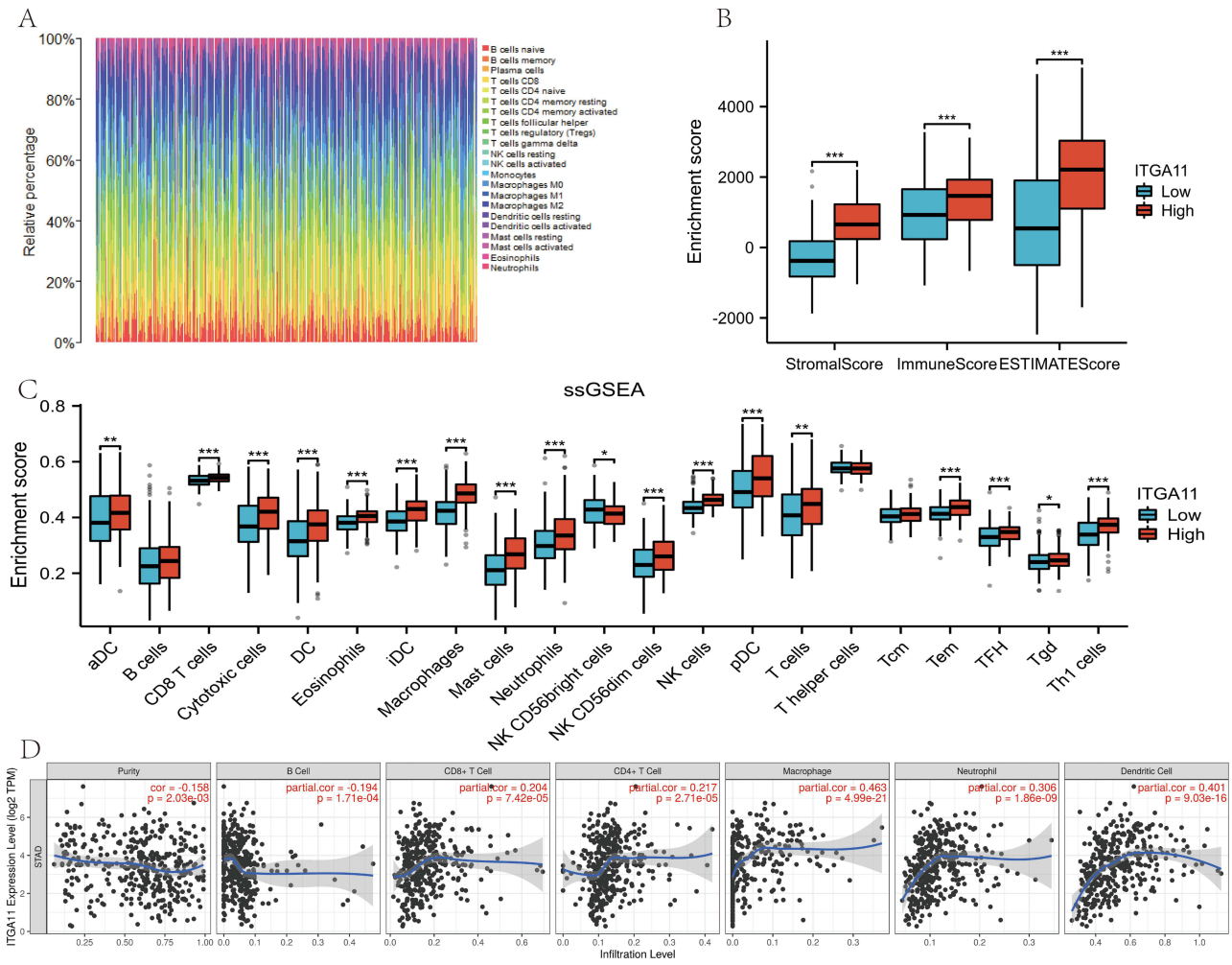

Figure 4 The relationship between ITGA11 and immune infiltration. (**A**) The proportion of infiltrating immune subsets in STAD. (**B**) The association between immune infiltration and ITGA11 expression according to ESTIMATE, immune, and stromal scores. (**C**) Differences in immune cell infiltration according to ITGA11 expression. (**D**) Correlation analyses between ITGA11 expression and CD8 active T cells, CD4 active T cells, macrophages, neutrophils, and dendritic cells. ITGA11 was inversely correlated with memory B cells. *p < 0.05; **p < 0.01, ***p < 0.001.

Abbreviations: ITGA11, Integrin subunit alpha 11; STAD, stomach adenocarcinoma.

COL3A1, FN1, COL1A1, COL1A2, SPARC, and *DCN* (Figure 6A). These hub genes were all identified as independent risk factors for prognosis in STAD, and seven were directly linked to survival outcomes (Figure 6B–L). *MMP2, COL3A1, COL1A2*, and prognosis were not statistically significantly different.

Prediction of Antineoplastic Drug Response

The drug sensitivity to antineoplastic drugs in two distinct ITGA11 expression groups (cut-off: 50%) was assessed to develop personalized treatment plans. The high-ITGA11 expression group had higher IC_{50} values for the antineoplastic drugs afatinib, cytarabine, dabrafenib, entinostat, erlotinib, gefitinib, ibrutinib, lapatinib, leflunomide, osimertinib, oxaliplatin, and sorafenib than the low-ITGA11 expression group (Figure 7A–L). These findings suggested that high-ITGA11 expression patients with STAD might benefit less from targeted therapy.

ITGA11 Expression in STAD Tissues Compared to Normal Tissues

ITGA11 expression and distribution in tumor tissue compared to the adjacent noncancerous tissue were examined using PCR and IHC. Analysis of the RNA expression in 31 fresh gastric cancer cases and the adjacent noncancerous tissues revealed higher *ITGA11* mRNA expression in the gastric cancer tissues (Figure 8A). Figure 8D demonstrates

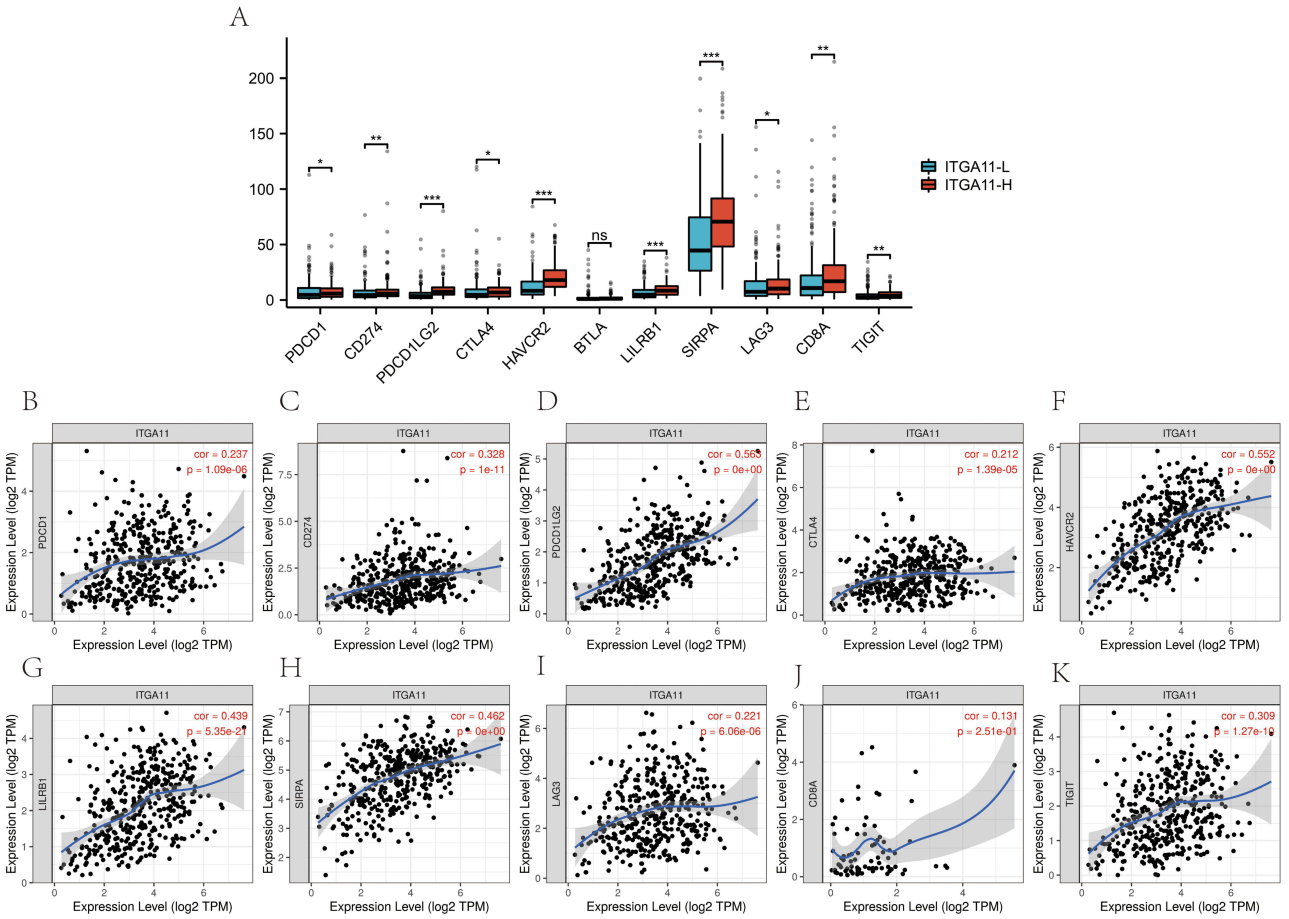

Figure 5 Identification of ITGA11-related immune checkpoints in STAD. (**A**) Comparison of immune checkpoint expression according to ITGA11 expression. Spearman correlation analysis between ITGA11 expression and PDCD1 (**B**), CD274 (**C**), PDCD1LG2 (**D**), CTLA4 (**E**), HAVCR2 (**F**), LILRB1 (**G**), SIRPA (**H**), LAG3 (**I**), CD8A (**J**), and TIGIT (**K**). *p < 0.05; **p < 0.01, ***p < 0.001.
Abbreviations: ns, no significance; ITGA11, Integrin subunit alpha 11; STAD, stomach adenocarcinoma.

that the gastric cancer tissues had significantly higher ITGA11 expression levels (Figure 8E and F) than the adjacent tissues (Figure 8B and 8C). This result highlighted the notable upregulation of ITGA11 expression in gastric cancer tissue compared to the adjacent noncancerous tissue and emphasized its potential significance in gastric cancer development.

Discussion

Recently, it was reported that ITGA11 was dysregulated and associated with poor prognosis in diverse cancers.[22] ITGA11 expression is high in non-small cell lung cancer, esophageal cancer, colorectal adenocarcinoma, and breast cancer, driving cancer cell proliferation, migration, and invasion, which are closely linked to tumor recurrence.[7,11–13] In the present study, bioinformatics analysis of STAD tissues revealed significantly elevated ITGA11 expression compared to that in paracancerous tissues. Patients with STAD with ITGA11 overexpression had a lower survival rate, indicating that ITGA11 is a robust diagnostic and prognostic indicator. Correlation analyses of clinicopathological parameters revealed a significant link between high ITGA11 expression, invasion depth, and patients' survival status. Both univariate and multivariate analyses suggested the potential of ITGA11 as an independent prognostic factor for gastric cancer. Thus, ITGA11 might be a new potential STAD diagnosis and prognosis biomarker.

The ITGA11-associated DEGs in STAD underwent GO/KEGG and GSEA functional enrichment analysis to predict ITGA11 function. The analysis revealed ITGA11 involvement in STAD tumor progression, immune system

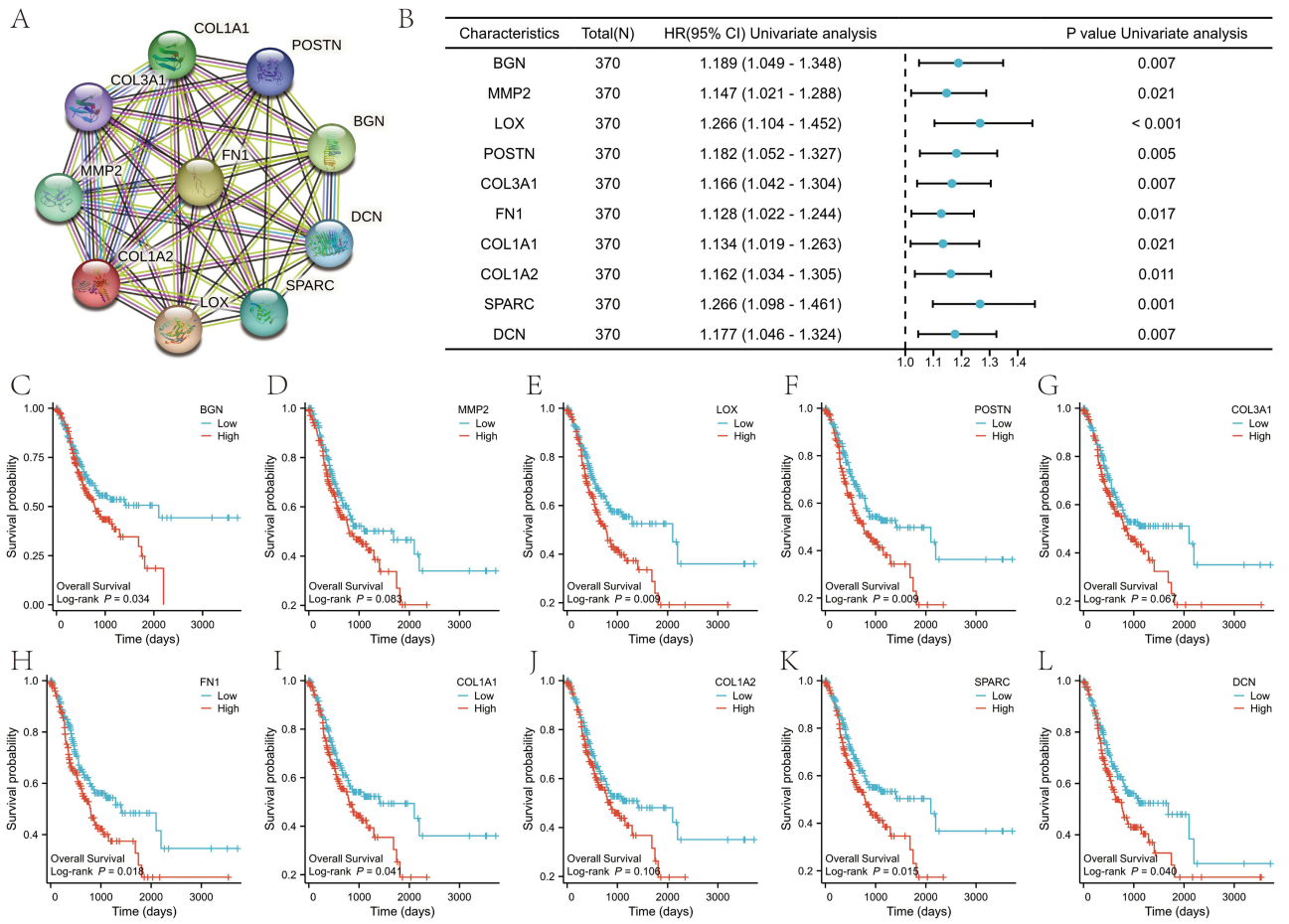

Figure 6 Interaction and prognostic value of the top 10 hub genes. (**A**) Protein–protein interaction (PPI) network. (**B**) The forest plot of the COX analysis of hub gene expression. Kaplan–Meier survival analysis of BGN (**C**), MMP2 (**D**), LOX (**E**), POSTN (**F**), COL3A1 (**G**), FN1 (**H**), COL1A1 (**I**), COL1A2 (**J**), SPARC (**K**), and DCN (**L**). **Abbreviations**: HR, hazard ratio; CI, confidence interval.

activation, tumorigenesis mechanisms, PI3K–AKT pathway activation, and other signaling cascades. Furthermore, ssGSEA demonstrated that high ITGA11 expression correlated with increased CD8+ T cell, macrophage, dendritic cell, and NK cell infiltration. Therefore, ITGA11 is closely related to regulating the tumor immune microenvironment and promotes tumor progression by participating in coordinating antigen presentation, cellular immunity, and humoral immunity. Immunity is critical in tumor promotion and tumor protection.[23] Cancer cells exploit signaling pathways to induce checkpoint molecule overexpression and reduce autoimmune response amplitude, thereby suppressing tumor immunity, which is a key immune resistance mechanism.[24,25] Therefore, searching for immune-related biomarkers is critical to developing new cancer therapies. In the present study, correlation analysis demonstrated a positive association between ITGA11 and immune checkpoint expression levels (PDCD1, CD274, PDCD1LG2, CTLA4, HAVCR2, LILRB1, SIRPA, LAG3, CD8A, and TIGIT). Thus, high ITGA11 expression might have a better effect on immune checkpoint inhibition.

The ITGA11 PPI network was predicted and constructed, and 10 hub genes that synergistically interact with ITGA11 were identified. *BGN, LOX, POSTN, FN1, COL1A1, COL1A2, COL3A1, SPARC*, and *MMP2* are highly expressed in gastric cancer and associated with poor prognosis.[26–33] These genes facilitate tumor progression by participating in collagen synthesis, extracellular matrix construction, CAF activation, promotion of tumor cell migration, local invasion, and lymph node metastasis.[31,34–40] These findings provided insight into the role of ITGA11 in STAD and directions for treatment.

Gastric cancer is frequently diagnosed at an advanced stage and has limited treatment options, primarily centered on cytotoxic chemotherapy. Currently, the HER2 antibody trastuzumab is the sole targeted therapy for gastric cancer,

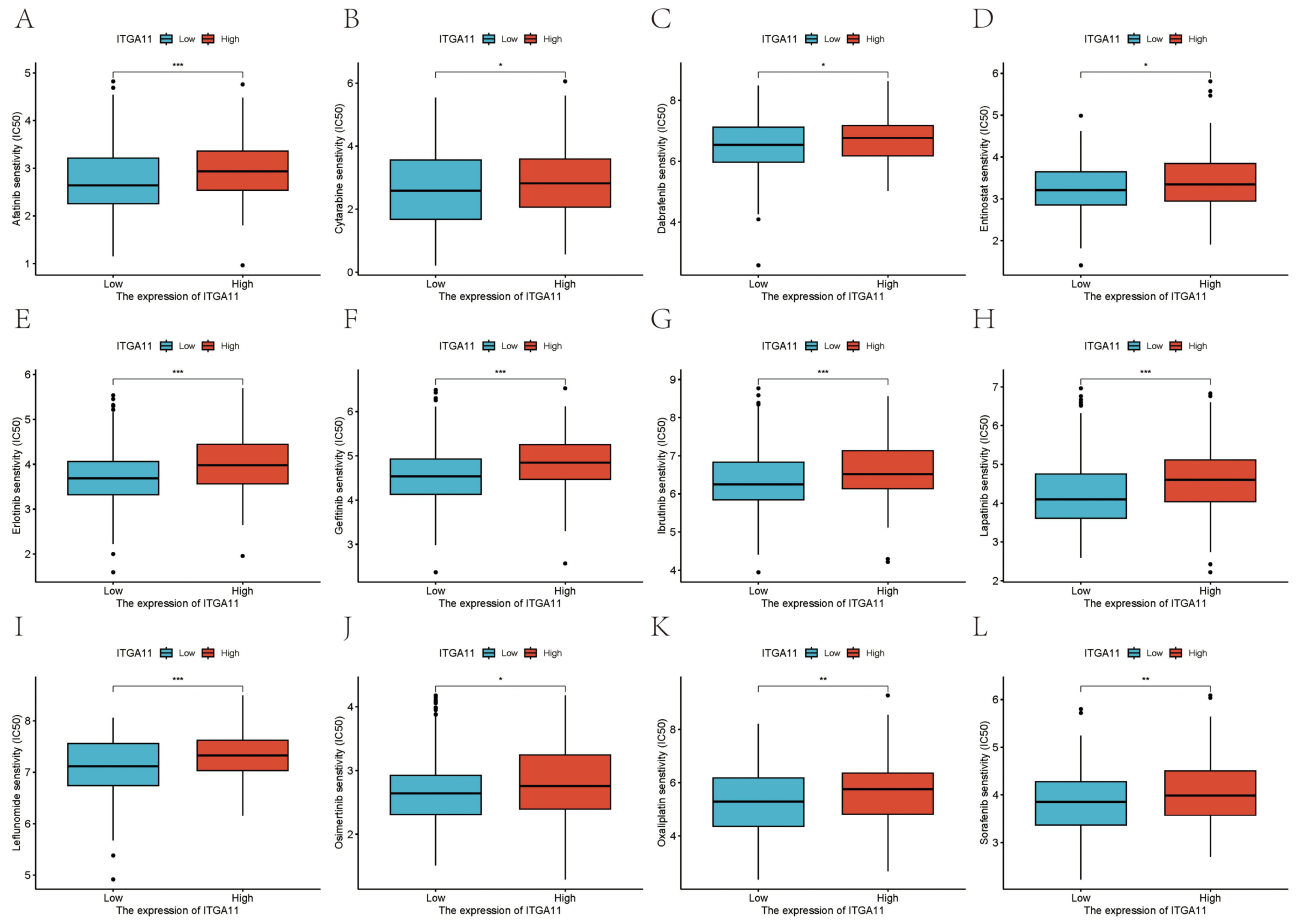

Figure 7 Drug sensitivity of ITGA11 in STAD. The predicted IC50 of Afatinib (**A**), cytarabine (**B**), dabrafenib (**C**), entinostat (**D**), erlotinib (**E**), gefitinib (**F**), ibrutinib (**G**), lapatinib (**H**), leflunomide (**I**), osimertinib (**J**), oxaliplatin (**K**), and sorafenib (**L**) according to ITGA11 expression. *p < 0.05; **p < 0.01, ***p < 0.001; ns, no significance.
Abbreviations: ITGA11, Integrin subunit alpha 11; IC50, median inhibitory concentration.

while the pan-HER inhibitor afatinib is under clinical investigation.[41] In the present study, drug sensitivity analysis based on ITGA11 expression level conducted to guide clinical treatment revealed that high ITGA11 expression correlated with reduced STAD sensitivity to oxaliplatin, the first-line chemotherapy drug, and afatinib, the pan-HER inhibitor.

The treatment landscape for advanced gastric cancer presents significant challenges, necessitating the exploration of novel anti-tumor therapeutic agents. Given the increased expression of immune checkpoints, immunosuppression appears promising as a breakthrough for treating patients with STAD with elevated ITGA11 expression. Finally, the present study confirmed the increased ITGA11 expression in tumor tissues through RT-qPCR and IHC, highlighting ITGA11 as an immune-related biomarker for diagnosing and prognosticating gastric cancer. The findings provided insight into ITGA11's function for future research on STAD.

The present study underscores the potential of ITGA11 as a diagnostic and prognostic marker for STAD. However, the study's limitations should be acknowledged. Although a correlation between ITGA11 and immune infiltration was established, the precise molecular mechanism remains elusive. The reduced sensitivity to oxaliplatin treatment among patients with high ITGA11 expression remains unverified experimentally. Lastly, the therapeutic approach for patients with elevated ITGA11 expression warrants further investigation.

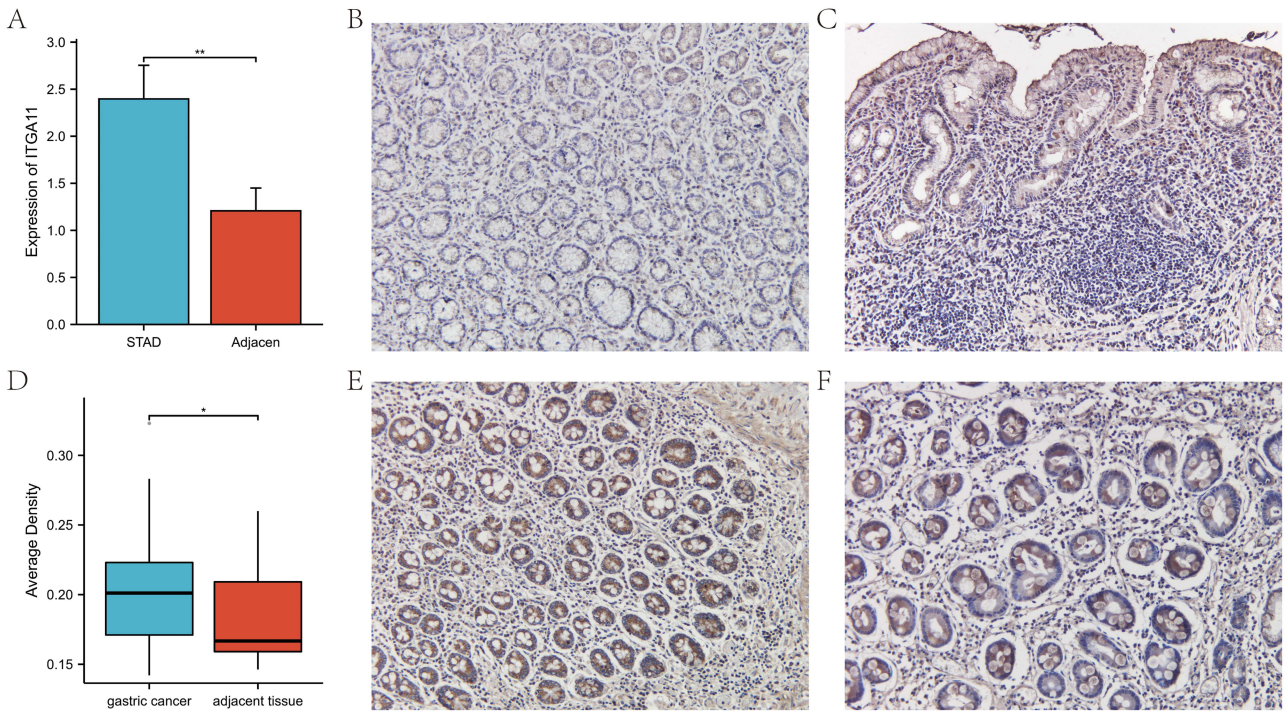

Figure 8 RT-qPCR and IHC of ITGA11 overexpression in STAD tissue compared to the adjacent noncancerous tissue. (**A**) RT-qPCR comparison of ITGA11 expression levels in STAD tissues versus adjacent noncancerous tissues. (**B** and **C**) Immunohistochemical images of ITGA11 expression in adjacent noncancerous tissue (×200). (**D**) IHC comparison of ITGA11 expression between STAD tissue and adjacent noncancerous tissue. (**E** and **F**) Immunohistochemical images of ITGA11 in STAD tissues (×200). *p < 0.05; **p < 0.01.

Abbreviations: ITGA11, Integrin subunit alpha 11; STAD, stomach adenocarcinoma; RT-qPCR, real-time quantitative polymerase chain reaction; IHC, immunohistochemistry.

Conclusion

ITGA11 is highly expressed in STAD and is a sensitive diagnostic and prognostic factor with potential as a therapeutic target for STAD. ITGA11 expression was associated with immune infiltration, which might promote STAD progression by influencing the tumor immune microenvironment.

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Disclosure

The authors declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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