Original Research

Abnormal TACC3 Expression is an Independent Prognostic Biomarker in Lung Carcinoma

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Abstract

Objective: Abnormal expression of transforming acidic coiled-coil protein 3 (TACC3) has been reported in many types of human malignancies. However, the expression of TACC3 and its clinical significance have not been well characterized in lung carcinoma (LUAD). The aim of this study was to investigate possible associations between tumor expression of TACC3 and the clinicopathological characteristics and prognosis of LUAD patients. **Methods**: The expression of TACC3 in LUAD patients was determined using the Oncomine, Gene Expression Profiling Interactive Analysis (GEPIA), UALCAN, and Cancer Genome Atlas (TCGA) databases. The expression of TACC3 in LUAD tissues was also determined by qRT-PCR. **Results**: TACC3 was found to be significantly overexpressed in LUAD tumors compared with non-tumor tissue in the above public databases. Receiver operating characteristic (ROC) curve analysis indicated that TACC3 could have diagnostic value in LUAD patients. Kaplan-Meier analysis further indicated that high TACC3 expression in tumors was significantly associated with worse overall survival (OS) in LUAD patients. In addition, univariate and multivariate Cox regression analyses showed that high TACC3 expression was an independent factor for worse OS in LUAD patients. Finally, based on gene set enrichment analysis (GSEA 3.0), we identified several potential pathways related to TACC3 that were enriched in the high TACC3 expression phenotype. **Conclusions**: The present study provides evidence that TACC3 expression is upregulated in LUAD and may be an independent risk factor for worse prognosis in these patients.

Keywords: TACC3; prognosis; survival; outcome; lung carcinoma (LUAD)

1. Introduction

Lung cancer, including mainly small cell lung cancer and non-small cell lung cancer (NSCLC), is the most common malignancy and causes a large number of deaths worldwide [1]. NSCLC includes adenocarcinoma, squamous and large cell lung cancer [2]. The 5-year overall incidence of lung carcinoma (LUAD) in China has remained low for the past 30 years [3]. Surgery, radiotherapy, chemotherapy, and targeted therapies are the first-line treatments for this cancer type. However, the above treatment strategies often have limited efficacy in locally advanced, metastatic and recurrent disease, and hence the treatment of LUAD requires new therapeutic approaches [4]. Exploration of the underlying mechanism of LUAD development and progression is therefore vital for the identification of novel therapeutic strategies.

TACC (transforming acidic coiled-coil protein) family members, including TACC1, TACC2 and TACC3, were first discovered in multiple myeloma [5]. In addition to maintaining centrosome microtubule nucleation and regulating centrosome integrity during mitosis [6], the TACC family has also been implicated in tumorigenesis. Recently, abnormal expression of TACC1 and/or TACC3 was observed in ovarian, breast, melanoma, bladder, NSCLC and prostate cancers [7–12]. Abnormal expression of TACC2 was also reported in prostate cancer [13], breast carcinoma and hepatocellular carcinoma [14,15]. Furthermore, fibroblast growth factor (FGFR) 1-TACC1 and FGFR3-TACC3 gene fusions, which are associated with aneuploidy and have oncogenic activities, have been reported in various cancer types [16,17]. These findings suggest that TACC3 may potentially contribute to tumorigenesis.

Mounting evidence has shown that TACC3 overexpression is associated with tumor aggressiveness and poor prognosis in prostate [8], breast [7], colorectal [9], gastric [10], and human renal cancers [18]. However, the expression status of TACC3 in LUAD remains largely unclear. Here, we investigated the relationship between TACC3 expression and the outcome of LUAD patients using bioinformatic analysis. Our findings indicate that TACC3 could serve as a potential prognostic biomarker in these patients.
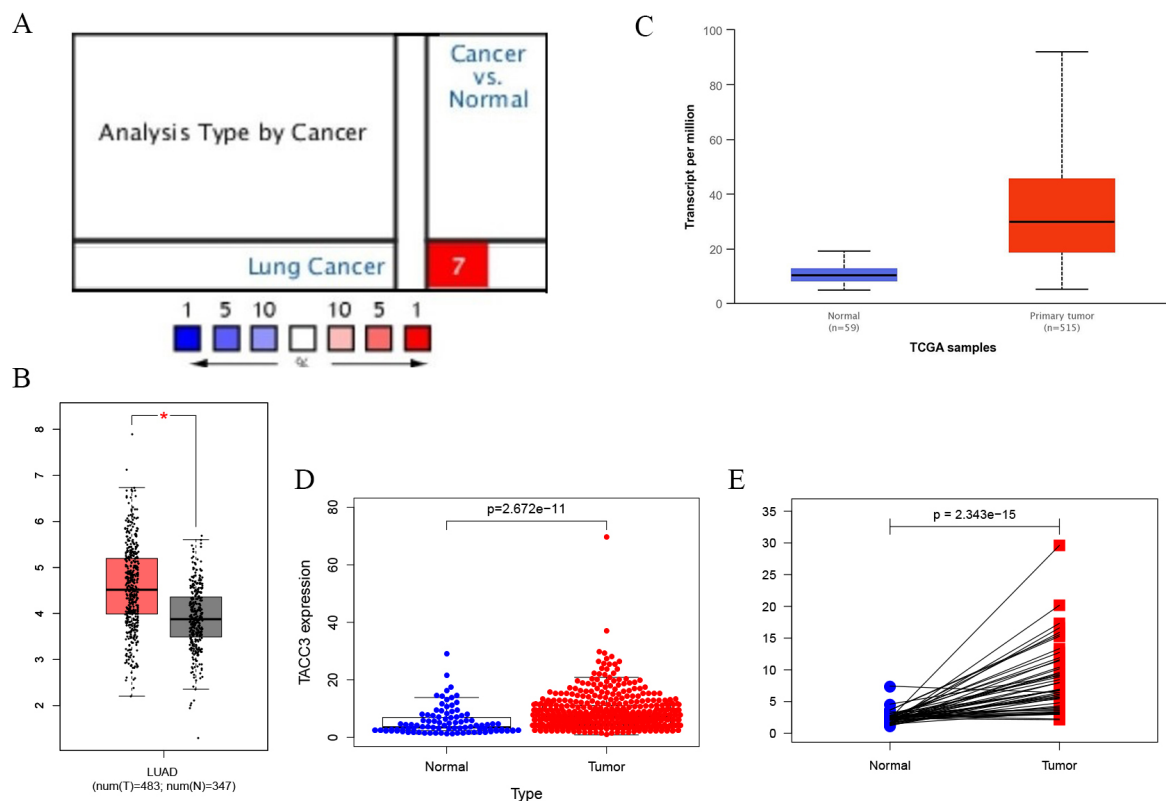
Fig. 1. TACC3 expression levels in LUAD cancer determined using four databases. (A) Oncomine database. Cell color is determined by the best gene rank percentile for the analyses within the cell. (B) GEPIA database. Significant differences between cancer types are shown in red, $p < 0.05$. (C) UALCAN database. Normal vs tumor, $p = 1.6235e\text{-}12$. (D) TCGA database analyzed by R script. $p = 2.672e\text{-}11$. (E) TACC3 expression in a paired comparison of LUAD and adjacent normal tissues. Data was extracted from the TCGA database, $p = 2.343e\text{-}15$.

2. Materials and Methods

2.1 Tissue Specimens

Fresh tissue (n = 6) with histologically confirmed cancer was obtained from LUAD patients who had not undergone any prior treatments and who were admitted to the Fourth Hospital of Hebei Medical University.

2.2 Oncomine Database Analysis

The Oncomine database is a powerful set of analysis functions that compute gene expression signatures, clusters and gene-set modules, thus automatically extracting biological insights from 715 datasets and 86,733 samples (https://www.oncomine.org/resource/login.html) [19]. The expression levels of TACC3 in LUAD were determined here by Oncomine Database analysis. The following threshold was considered as statistically significant: $p = 0.0001$, fold change = 1.5, gene rank = all.

2.3 GEPIA Database Analysis

GEPIA (http://gepia.cancer-pku.cn/) is a newly developed interactive web server for analyzing RNA sequence expression data for 9736 tumor and 8587 normal samples from the TCGA and GTEx projects using a standard processing pipeline [20]. TACC3 expression in LUAD was determined in the single gene expression analysis using the following thresholds: $|\log_2|FC$ cutoff = 0.5 and p-value cutoff = 0.01. In the survival analysis, the threshold was determined according to the following values: group cutoff: median; cutoff-high (%) and cutoff-low (%): 50 and 50.

2.4 UALCAN Database Analysis

UALCAN is a comprehensive and interactive web resource (http://ualcan.path.uab.edu/index.html) designed to provide easy access to publicly available cancer OMICS data (TCGA and MET500), thus facilitating the identification of candidate biomarkers. The expression of TACC3 and patient survival data were selected from the TCGA databases, with $p < 0.05$ considered significant.

2.5 TCGA Database Analysis

Gene expression and patient data for LUAD were downloaded from Genomic Data commons (GDC) (https://portal.gdc.cancer.gov/) using the GDC data transfer tool. Gene expression data were analyzed by R (version: 3.6.1, Boston, MA, USA) with related R packages. Clinical parameters such as age, gender, survival status, and tumor
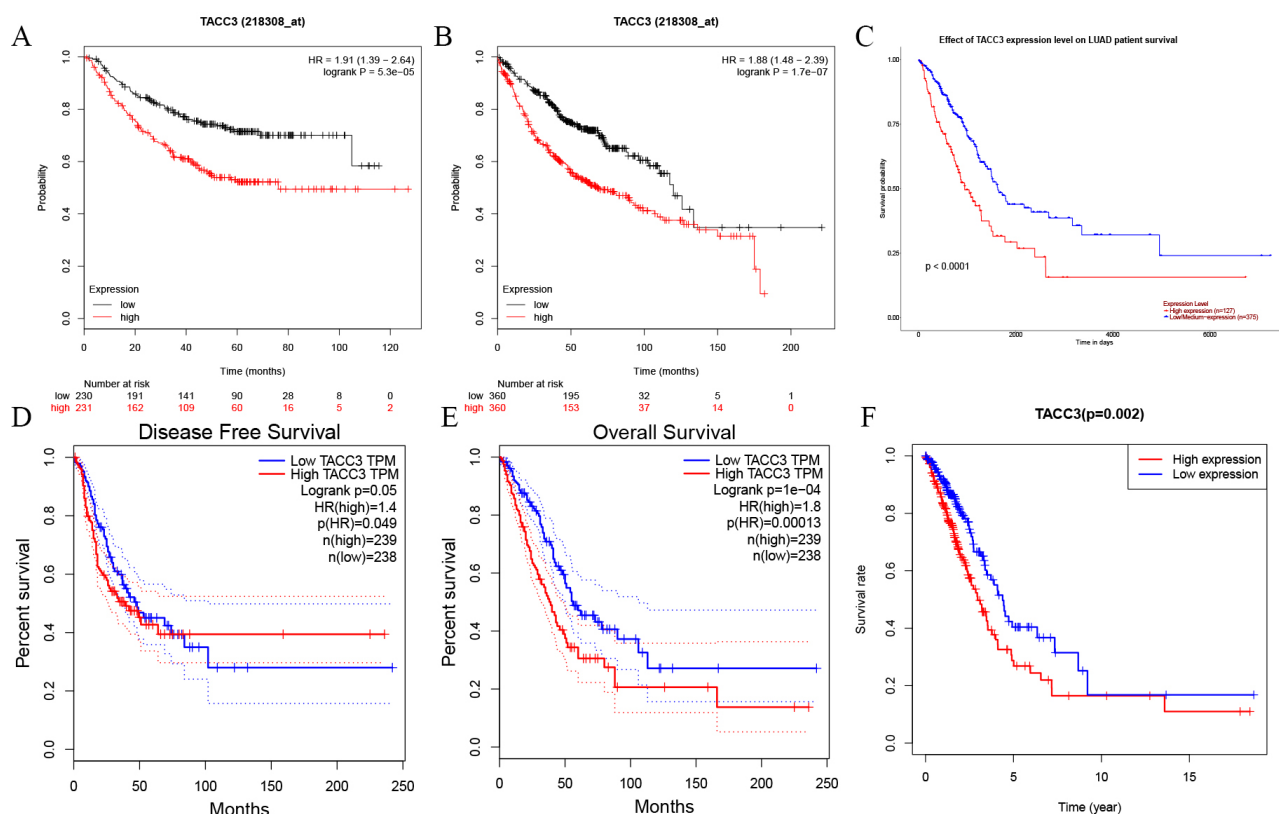
Fig. 2. Kaplan-Meier survival curves for TACC3 expression in LUAD as determined using four databases. (A,B) OS and RFS from Kaplan-Meier Plotter database. (C,D) OS and DFS from GEPIA database. (E) OS from UALCAN database. (F) OS from TCGA database. OS, Overall Survival; RFS, Relapse-Free Survival; DFS, Disease Free Survival.

stage were extracted from the patient data and matched to each patient using the PERL script.

2.6 Kaplan-Meier Plotter Database Analysis

Based on a meta-analysis, the Kaplan Meier plotter (http://kmplot.com/analysis/) is capable of assessing the association of 54,000 genes with patient survival in 21 cancer types [21,22]. The correlation between TACC3 expression and overall survival (OS) in LUAD, as well as with First Progression (FP), was analyzed using mRNA data. Patients were divided according to the median value, with the cutoff value set as auto select.

2.7 ROC Curve Generation

To assess the diagnostic value of TACC3, ROC curves were generated using SPSS 26 (IBM SPSS Statistics, Chicago, IL, USA). The AUC was determined and is shown for each panel.

2.8 Kyoto Encyclopedia of Genes and Genomes (KEGG) Analysis

To identify potential mechanisms that underlie the associations of TACC3 expression in LUAD, KEGG analysis was performed to determine whether an *a priori* defined set of genes was differentially expressed between high and low

TACC3 expression groups [23]. Gene sets with a normal *p*-value of <0.05 and false discovery rate (FDR) of <0.05 were considered to be significantly enriched.

2.9 RNA Extraction and qRT-PCR Methods

qRT-PCR was performed to determine the expression of TACC3 mRNA. Briefly, total RNA from the surgically obtained paired (tumor and normal) tissues (n = 6) was isolated using the TRI Reagent RNA Isolation Reagent (Sigma-Aldrich) according to the manufacturer's instructions. The first-strand template complementary DNA (cDNA) was synthesized using a reverse transcription kit (Takara, Japan). The primer sequences were as follows: TACC3: 5'-CCTCTTCAAGCGTTTTGAGAAAC-3' (sense) and 5'-GCCCTCCTGGGTGATCCTT-3' (antisense); β-actin: 5'- CGCGAG AAGATGACCCAGAT-3' (sense) and 5'-GGGCATACCCCT CGTAGATG-3' (antisense) [10,18]. β-actin was used as the internal control. The PCR reaction was performed as follows: denaturation at 94 °C for 3 minutes, and then 35 cycles of 94 °C for 30 seconds, 56 °C for 30 seconds, 72 °C for 2 minutes, and finally an elongation step at 72 °C for 10 minutes. Three independent experiments were performed.
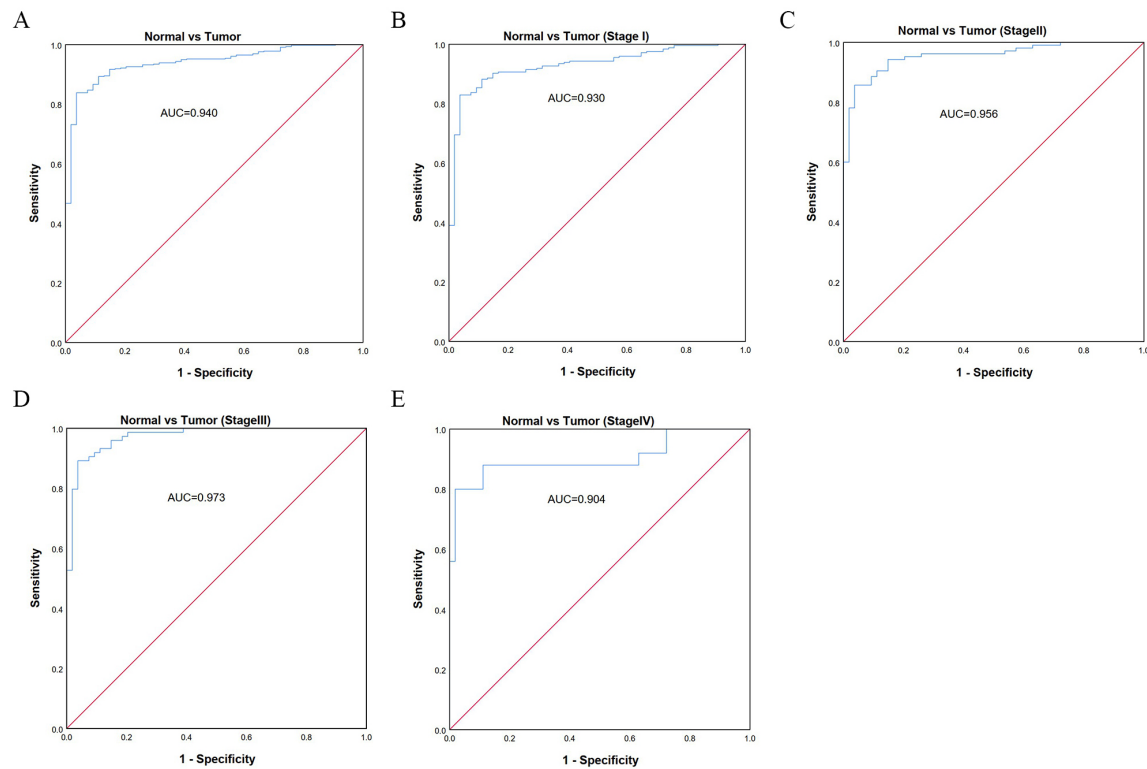
Fig. 3. Diagnostic value of TACC3 expression in LUAD using ROC analysis. (A) ROC curve for TACC3 mRNA expression in normal and LUAD tissues. (B–E) ROC curves for TACC3 mRNA expression in different stages (I, II, III, IV) of LUAD. All AUCs are shown for each ROC curve. AUC, area under ROC curve.
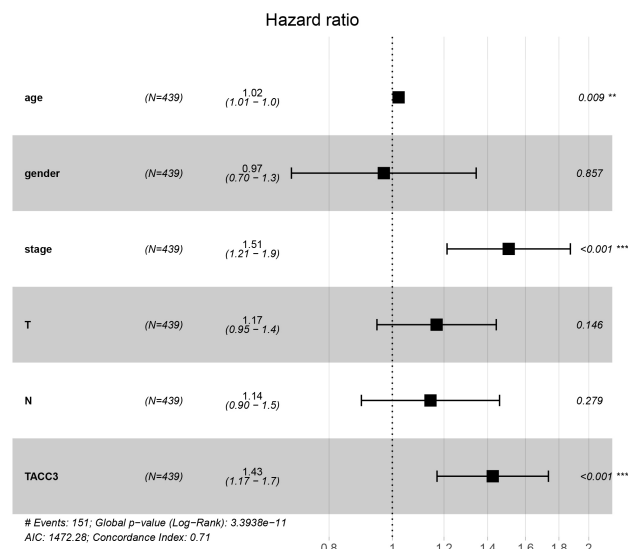

Fig. 4. Multivariate Cox regression analysis shows that TACC3 is an independent risk factor for OS among LUAD patients. $**p < 0.01$, $***p < 0.001$.

2.10 Statistical Analysis

All analyses of the TCGA data were conducted using R software (version 3.6.1). Univariate Cox regression analysis was used to select potential prognostic factors, and multivariate Cox analysis was performed to determine the correlation between TACC3 expression and survival, as well as with other clinical features. Statistical analyses were performed using SPSS 26 (IBM SPSS Statistics, USA), with $p < 0.05$ considered to be statistically significant.

3. Results

3.1 Characteristics of LUAD Patients from the TCGA

Clinical data for 467 patients was downloaded from the TCGA database and included age, gender, stage, TMN classification and survival status (Table 1).

3.2 High TACC mRNA Expression in LUAD

TACC3 mRNA expression in LUAD was determined from the Oncomine, GEPIA and UALCAN databases. The level of TACC3 expression was higher in LUAD tissues compared with normal tissues (Fig. 1A–C). These results were further confirmed by analysis of the TCGA database ($p = 2.672$e-11, Fig. 1D). In addition, a significant difference in TACC3 expression was observed in a paired comparison of LUAD with adjacent normal tissues ($p = 2.343$e-15, Fig. 1E). These results demonstrate that TACC3 was highly expressed in LUAD compared with normal tissues.
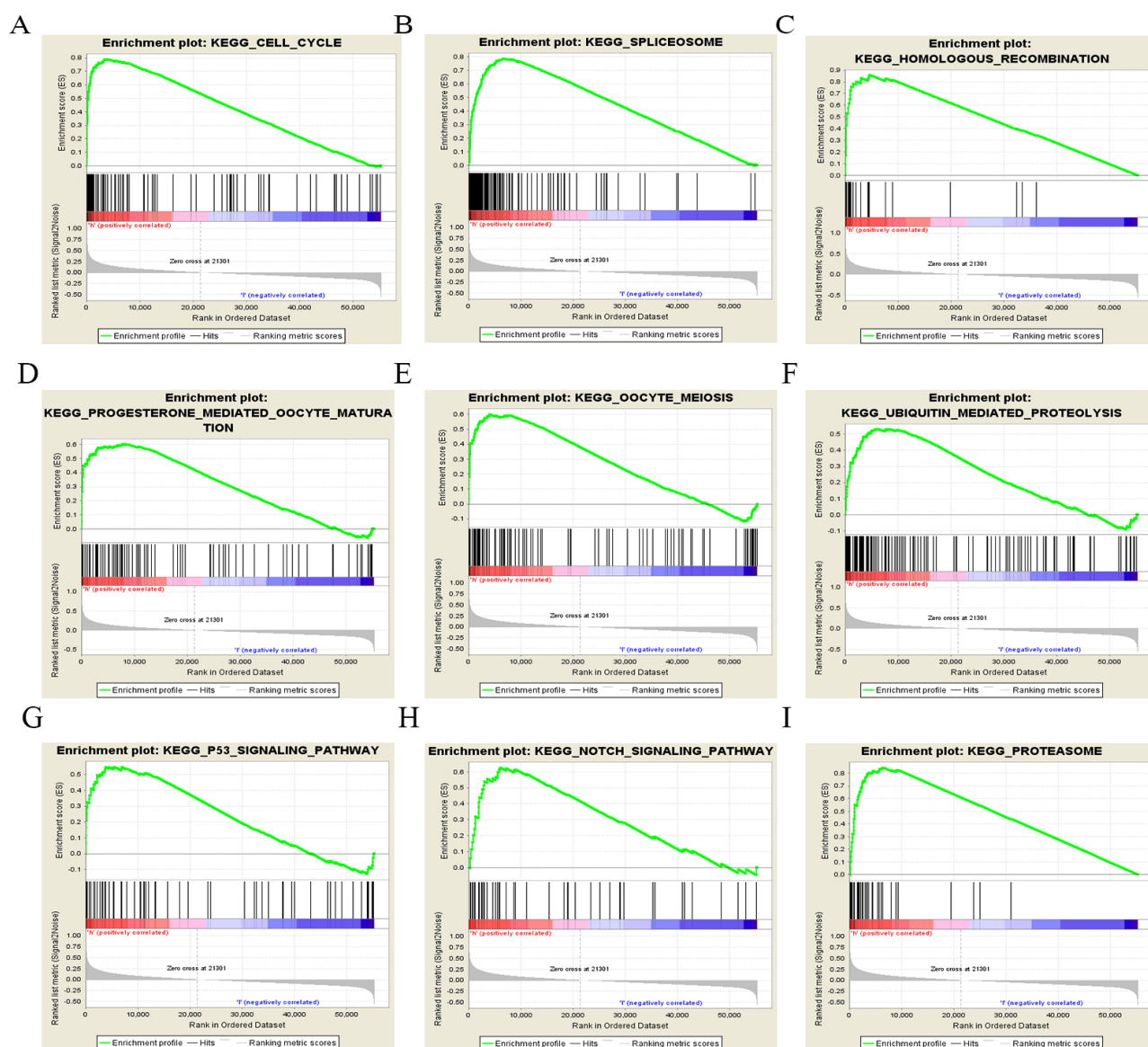
Fig. 5. Enrichment plots for LUAD cases with high TACC3 expression using GSEA 3.0. GSEA results showing differential enrichment of genes related to various pathways. (A) Cell cycle. (B) Spliceosome. (C) Homologous recombination. (D) Progesterone-mediated oocyte maturation. (E) Oocyte meiosis. (F) Ubiquitin-mediated proteolysis. (G) p53 signaling pathway. (H) Notch signaling pathway. (I) Proteasome.

3.3 Prognostic Value of TACC3 in LUAD

The prognostic value of TACC3 expression in LUAD patients was determined using the Kaplan-Meier Plotter, GEPIA, UALCAN, and TACG databases. No significant difference was observed for disease free survival (DFS) with GEPIA (Log rank $p = 0.05$, HR = 1.4; Fig. 2D). However, high TACC3 mRNA expression was significantly associated with poor OS of LUAD patients in Kaplan-Meier Plotter (Log rank $p = 1.7$e-07, HR = 1.88; Fig. 2B), UAL-CAN ($p < 0.0001$; Fig. 2C), GEPIA (Log rank $p = 1$e-04, HR = 1.8; Fig. 2E), and TCGA ($p = 0.002$; Fig. 2F) when analyzed by R. In addition, high TACC3 mRNA expression in LUAD patients was significantly associated with worse

FP in Kaplan-Meier Plotter (Log rank $p = 5.3$e-05, HR = 1.91; Fig. 2A). These results indicate that TACC3 expression has a major impact on the survival of LUAD patients.

3.4 Association of TACC3 Expression with Survival in Clinical Subgroups of LUAD Patients

The relationship between TACC3 expression and the survival of various clinicopathological subgroups of LUAD patients was determined using Kaplan-Meier plotter. As shown in Table 2, TACC3 mRNA expression was negatively associated with OS in both female and male patients ($p = 0.0084$, $p = 9.1$e-4, respectively), as well as in LUAD patients who were smokers ($p = 0.008$). High expression
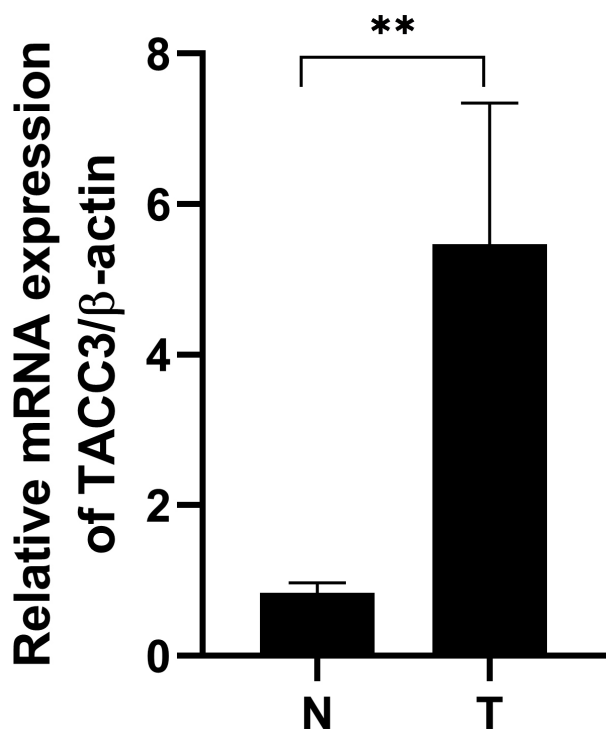
Fig. 6. TACC3 mRNA expression is upregulated in LUAD tissue compared to adjacent normal tissue. T: LUAD tissues; N: noncancerous tissues. The results shown are the mean $\pm$ SD from six paired samples. $**p < 0.01$.

of TACC3 was also associated with worse OS in stage 1, 3, AJCC stage T1, stage N0, and M0 patients ($p = 9.7$e-5, $p = 0.023$, $p = 5.2$e-4, $p = 0.0035$ and $p = 7.6$e-4, respectively). TACC3 expression was also associated with FP in males, non-smokers, and stage 1 LUAD patients ($p = 5.1$e-4, $p = 0.027$ and $p = 0.0058$, respectively). No significant associations were observed between TACC3 expression and the PPS of LUAD patients. These results suggest that TACC3 expression is mainly associated with OS in LUAD patients.

3.5 Diagnostic Value of TACC3 Expression in LUAD Patients

ROC analysis was performed to assess the diagnostic value of TACC3 expression in LUAD patients. The observed AUC of 0.940 suggests that TACC3 mRNA expression has strong diagnostic value for LUAD (Fig. 3A). We further examined the diagnostic value of TACC3 in stage I, II, III, and IV LUAD patients (Fig. 3B–E). These showed AUCs of 0.930, 0.956, 0.973, and 0.904, respectively, indicating that TACC3 is a potential diagnostic biomarker for LUAD.

3.6 High TACC3 Expression is an Independent Risk Factor for Worse OS in LUAD Patients

We next performed univariate and multivariate Cox regression analyses using R script to determine whether TACC3 expression was an independent risk factor for OS in

Table 1. Clinical characteristics of the 467 LUAD patients downloaded from the TCGA database.

Characteristic	N (%)
Age (years)	
≤ 60	155 (33.19)
>60	312 (66.81)
Gender	
Female	254 (54.39)
Male	213 (45.61)
Stage	
I	251 (53.75)
II	108 (21.13)
III	75 (16.06)
IV	25 (5.35)
Not available	8 (3.71)
T classification	
T1	162 (34.69)
T2	244 (52.25)
T3	39 (8.35)
T4	19 (4.07)
TX	3 (0.64)
M classification	
M0	314 (67.24)
M1	24 (5.14)
MX	125 (26.77)
Not available	4 (0.85)
N classification	
N0	300 (64.24)
N1	87 (18.63)
N2	66 (14.13)
N3	2 (0.43)
NX	11 (2.36)
Not available	1 (0.21)
Survival status	
Deceased	158 (33.83)
Alive	309 (66.17)

LUAD patients. Stage, T and N classification, and TACC3 expression were all independent risk factors for OS in univariate Cox analysis ($p = 3.07$e-11, 2.24e-5, 7.17e-9, and 8.23e-3, respectively; Table 3). In multivariate Cox analysis, only stage and TACC3 expression were identified as independent risk factors ($p = 2.2$e-4 and $p = 4.1$e-4, respectively). These results indicate that TACC3 expression is an independent risk factor for worse OS in LUAD patients (HR = 1.43, 95% CI: 1.17– 1.7, $p < 0.001$; Fig. 4).

3.7 High Expression of TACC3 mRNA in LUAD Tissue

Real-Time PCR was performed to determine TACC3 mRNA levels in 6 pairs of matched LUAD tissues and their adjacent non-cancerous tissues. The expression of TACC3 mRNA was upregulated in LUAD cancer tissues compared to adjacent noncancerous tissues ($p < 0.01$, Figs. 5,6).

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Table 2. Correlation of TACC3 mRNA expression with prognosis in different clinicopathological subgroups of LUAD as determined by Kaplan-Meier plotter.

Clinicopathological characteristics	OS			FP			PPS		
	N	HR (95% CI)	Log rank p	N	HR (95% CI)	Log rank p	N	HR (95% CI)	Log rank p
Gender									
Female	318	1.67 (1.14–2.46)	0.0084**	235	1.52 (0.96–2.4)	0.071	59	1.19 (0.6–2.38)	0.62
Male	344	1.75 (1.25–2.44)	9.1e-4***	226	2.16 (1.38–3.37)	5.1e-4***	125	0.72 (0.38–1.37)	0.32
Smoking history									
Never smoked	22	1.47 (0.2–10.89)	0.7	143	2.01 (1.07–3.78)	0.027*	41	0.62 (0.26–1.48)	0.27
Smoked	246	1.91 (1.17–3.11)	0.008**	461	1.51 (0.97–2.33)	0.064	82	0.84 (0.47–1.48)	0.54
Stage									
1	370	2.25 (1.48–3.42)	9.7e-5***	283	1.99 (1.21–3.27)	0.0058**	66	1.06 (0.53–2.1)	0.88
2	105	1.62 (0.93–2.80)	0.085	103	0.94 (0.54–1.64)	0.84	38	0.52 (0.23–1.15)	0.099
3	24	3.54 (1.11–11.26)	0.023*	10	-	-	1	-	-
4	4	-	-	0			0	-	-
AJCC stage T									
1	123	3.18 (1.6–6.32)	5.2e-4***	47	1.56 (0.35–7)	0.56	7		
2	105	1.62 (0.93–2.8)	0.085	93	1.62 (0.86–3.06)	0.13	38	0.52 (0.23–1.15)	0.099
3	4	-	-	2	-	-	1	-	-
4	0	-	-	0	-	-	0	-	-
AJCC stage N									
0	184	2.07 (1.26–3,4)	0.0035**	102	1.31 (0.61–2.84)	0.49	25	0.73 (0.27–1.95)	0.53
1	44	1.15 (0.53–2.49)	0.72	38	1.24 (0.5–3.06)	0.65	19	-	-
2	3	-	-	2	-	-	2	-	-
AJCC stage M									
0	231	1.99 (1.32–2.99)	7.6e-4***	142	1.73 (0.97–3.09)	0.06	46	0.62 (0.3–1.28)	0.19
1	1	-	-	0	-	-	0	-	-

- Sample number too low for meaningful analysis. *$p < 0.05$, **$p < 0.01$, ***$p < 0.0001$.

Table 3. Univariate and multivariate analysis of clinicopathological factors and of TACC3 expression with OS in LUAD patients.

Parameter	Univariate analysis			Multivariate analysis		
	p-value	HR	95% CI	p-value	HR	95% CI
Age	1.01	1.00–1.03	0.15			
Gender	1.08	0.79–1.49	0.62			
Stage	1.65	1.43–1.92	3.07e-11****	1.51	1.21–1.87	2.2e-4***
T classification	1.53	1.26–1.87	2.24e-5****	1.16	0.94–1.44	0.15
N classification	1.70	1.42–2.03	7.17e-9****	1.14	0.90–1.46	0.28
TACC3	1.02	1.01–1.04	0.00823**	1.43	1.17–1.70	4.1e-4***

HR, hazard ratio; CI, confidence interval. **values indicate $p < 0.01$, ***values indicate $p < 0.001$, ****values indicate $p < 0.0001$.

4. Discussion

Increasing evidence suggests that TACC3 is associated with various types of human cancers, including breast [7,24,25], prostate [8], colorectal [9], bladder [26], gastric [10], ovarian [27], melanoma [28], and liver [29] cancers. However, little is known about the expression of TACC3 in LUAD. Recently, genomic alterations in members of the FGFR family were reported in several tumor types including breast, bladder, prostate, and lung cancer. FGFR3-TACC3 fusions have also been identified as novel genomic alterations in LUAD, mostly in patients who were never or limited smokers [16]. These results suggest that TACC3 could play an important role in LUAD progression. The present study demonstrated a significant relationship between TACC3 expression and patient survival in LUAD. This was further validated using Cox regression and ROC curve analyses.

Various databases including Oncomine, TMIER, Kaplan-Meier plotter, GEPIA, UALCAN, and TCGA were analyzed in this study to evaluate the prognostic significance of TACC3 expression in LUAD. Although different databases and methods were used, similar results were obtained. Our study found that abnormally high TACC3 expression in LUAD was associated with the poor survival

Table 4. KEGG pathways in the high TACC3 expression phenotype.

GENE set name	NES	NOM p-val	FDR q-val
KEGG_CELL_CYCLE	2.51	0	0
KEGG_SPLICEOSOME	2.47	0	0
KEGG_HOMOLOGOUS_RECOMBINATION	2.32	0	0
KEGG_PROGESTERONE_MEDIATED_OOCYTE_MATURATION	2.31	0	0
KEGG_OOCYTE_MEIOSIS	2.29	0	0
KEGG_NUCLEOTIDE_EXCISION_REPAIR	2.25	0	0
KEGG_PYRIMIDINE_METABOLISM	2.24	0	0
KEGG_BASE_EXCISION_REPAIR	2.22	0	0
KEGG_MISMATCH_REPAIR	2.22	0	0
KEGG_DNA_REPLICATION	2.18	0	0.001
KEGG_GLYOXYLATE_AND_DICARBOXYLATE_METABOLISM	2.18	0	0.001
KEGG_RNA_DEGRADATION	2.16	0	0.001
KEGG_UBIQUITIN_MEDIATED_PROTEOLYSIS	2.14	0	0.001
KEGG_P53_SIGNALING_PATHWAY	2.09	0	0.003
KEGG_BASAL_TRANSCRIPTION_FACTORS	2.07	0	0.003
KEGG_NOTCH_SIGNALING_PATHWAY	2.07	0	0.003
KEGG_AMINOACYL_TRNA_BIOSYNTHESIS	2.07	0	0.003
KEGG_PROTEASOME	2.06	0	0.003
KEGG_PATHOGENIC_ESCHERICHIA_COLI_INFECTION	2.05	0	0.003
KEGG_SMALL_CELL_LUNG_CANCER	2.04	0	0.003
KEGG_PURINE_METABOLISM	2	0	0.006
KEGG_PATHWAYS_IN_CANCER	1.89	0	0.016
KEGG_CHRONIC_MYELOID_LEUKEMIA	2.05	0.002	0.003
KEGG_CYSTEINE_AND_METHIONINE_METABOLISM	1.94	0.002	0.012
KEGG_PANCREATIC_CANCER	1.93	0.002	0.012
KEGG_BLADDER_CANCER	1.93	0.002	0.012
KEGG_PENTOSE_PHOSPHATE_PATHWAY	1.93	0.002	0.012
KEGG_ENDOCYTOSIS	1.79	0.002	0.033
KEGG_RENAL_CELL_CARCINOMA	1.93	0.004	0.012
KEGG_ONE_CARBON_POOL_BY_FOLATE	1.92	0.004	0.012
KEGG_GLIOMA	1.9	0.004	0.015
KEGG_N_GLYCAN_BIOSYNTHESIS	1.86	0.006	0.019
KEGG_PROSTATE_CANCER	1.83	0.006	0.023
KEGG_GAP_JUNCTION	1.78	0.008	0.034
KEGG_GLYCOLYSIS_GLUCONEOGENESIS	1.78	0.008	0.034
KEGG_CYTOSOLIC_DNA_SENSING_PATHWAY	1.76	0.008	0.038
KEGG_LYSINE_DEGRADATION	1.95	0.01	0.012
KEGG_GALACTOSE_METABOLISM	1.72	0.01	0.045
KEGG_REGULATION_OF_ACTIN_CYTOSKELETON	1.78	0.012	0.034
KEGG_NEUROTROPHIN_SIGNALING_PATHWAY	1.77	0.012	0.036
KEGG_FC_GAMMA_R_MEDIATED_PHAGOCYTOSIS	1.84	0.015	0.023
KEGG_ERBB_SIGNALING_PATHWAY	1.72	0.016	0.044
KEGG_NON_SMALL_CELL_LUNG_CANCER	1.74	0.024	0.042
KEGG_ACUTE_MYELOID_LEUKEMIA	1.7	0.029	0.049
KEGG_RNA_POLYMERASE	1.7	0.033	0.049

NES, normalized enrichment score; NOM, nominal; FDR, false discovery rate. Gene sets with NOM p-value < 0.05 and FDR q-value < 0.25 were considered as significantly enriched.

of these patients, suggesting that TACC3 may play an important role in the progression of LUAD. Univariate and multivariate Cox analyses confirmed that TACC3 expression may be a valuable prognostic biomarker for LUAD, and ROC curve analysis strongly validated the diagnostic value of TACC3 in LUAD.

A growing number of studies have proposed possible mechanisms to explain the relationship between TACC3 expression and patient prognosis in malignant cancers. In cervical cancer, TACC3 may promote the epithelial-mesenchymal transition (EMT) phenotype through activation of the PI3K/AKT and ERK signaling pathways [11]. TACC3 knockdown was also shown to inactivate PI3K/AKT signaling in kidney renal clear cell carcinoma [18]. These studies suggest that TACC3 may promote the EMT phenotype in cancer cells by regulating PI3K/AKT signaling. However, in the current study we found no significant enrichment of PI3K/AKT signaling pathway genes in LUAD using GSEA3.0 software (UC San Diego, CA, USA). This discrepancy may be due to the different materials and raw data, and/or to the different analysis methods used in the present study. More experiments are required to investigate the possible involvement of TACC3 with EMT and PI3K/AKT signaling in LUAD. However, we found that other cancer-associated signaling pathways, including non-small cell lung cancer and small cell lung cancer, as well as other tumor types, were associated with the high TACC3 expression phenotype, indicating that TACC3 may also be involved in other cancer types (Table 4).

5. Conclusions

In conclusion, analysis of the Oncomine and TCGA databases revealed that a high level of TACC3 expression was associated with poor prognosis in LUAD. This result was further verified by Cox regression and ROC analysis. Therefore, TACC3 may be a clinically useful prognostic biomarker in LUAD patients.

Author Contributions

XZ, XF and DH designed the studies. XZ, XF, XL, YW and DH wrote the paper. Part of TAGA analysis were performed by YZ, YL, JZ and DH.

Ethics Approval and Consent to Participate

The study protocol was approved by the Institutional Research Ethics Committee of the Fourth Hospital of Hebei Medical University. All patients gave informed consent for the study.

Acknowledgment

Not applicable.

Conflict of Interest

The authors declare no conflict of interest.

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