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Clinicopathological features and prognostic significance of TAF1L in gastric cancer

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Abstract

Background TAF1L may play an important role in the occurrence and development of gastric cancer (GC), but the correlation between the expression of TAF1L and the clinicopathological factors and prognosis of GC is still unclear.

Methods A total of 1053 GC patients in Zhejiang Cancer Hospital between January 1st, 2018 to December 31th, 2019 were screened. Finally, 120 patients met the inclusion criteria. TAF1L expression was detected by immunohistochemistry, and the correlations of TAF1L in clinicopathological characteristics and prognosis were analyzed. TCGA GC dataset was used to perform further bioinformatics analysis.

Results In this study, TAF1L expression was evaluated in 120 clinical samples of GC. TAF1L expression was higher in tumor tissues and was associated with tumor differentiation ($p=0.046$), signet-ring cells ($p=0.043$), dMMR status ($p=0.011$), lympho-vascular invasion ($p=0.038$), and neural invasion ($p=0.005$) in our cohort. Cases with high expression of TAF1L presented worse mean OS than those with low expression (40.3 months vs. 51.8 months, $p=0.019$), and the difference was also significant in HER2-positive cases (20.9 months vs. 51.2 months, $p=0.007$) as well as pMMR cases (38.8 months vs. 51.6 months, $p=0.006$). Multivariate Cox regression analysis showed that TAF1L (HR = 2.044, 95%CI = 1.007–4.147, $p=0.048$) and HER2 status (HR = 2.383, 95%CI = 1.087–5.222, $p=0.030$) were independent prognosis factors of these patients. In subgroup analysis, TAF1L was the independent prognostic risk factor in HER2-positive patients (HR = 6.736, 95%CI = 1.373–33.032, $p=0.019$). and pMMR patients (HR = 2.291, 95%CI = 1.126–4.660, $p=0.022$). Besides, HER2 status was the independent prognostic risk factor in TAF1L-H patients (HR = 4.832, 95%CI = 1.908–12.239, $p=0.001$). TCGA dataset also indicated the higher expression of TAF1L in tumors than normal tissues ($p<0.001$). High TAF1L expression is linked to worse survival in MSS (11.0 months vs. 35.0 months, $p=0.0046$) groups, and is negatively associated with overall survival in HER2-positive cases (24.0 months vs. 57.0 months, $p=0.0039$).

Conclusion TAF1L is closely related to the occurrence and development of GC. Our results suggested that TAF1L is a significant biomarker for predicting prognosis of GC and may play an important role in immunotherapy and targeted therapy.

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Keywords TAF1L, Gastric cancer, Clinicopathological features, Prognosis, Biomarker

Introduction

Gastric cancer (GC) is a common malignancy globally, and a serious threat to human health [1]. With the continuous improvement of diagnosis and treatment techniques, the comprehensive treatment level of gastric cancer has made some progress, but the overall efficacy is still less than satisfactory, and new therapeutic targets need to be further explored [2, 3].

TAF1 (TATA-box binding proteinassociated factor 1) which is also called TAF(II)250, is located on the X chromosome (Xq13.1), and encodes TATA box binding protein-associated factor 1 protein as a scaffold for TF II D which is involved in the transcription process of numerous genes in eukaryotic cells [4, 5]. As a homologue of TAF1, TAF1L (TATA-box binding protein associated factor 1 like) has been found that presents a similar function with histone acetyltransferase activity like TAF1 [6, 7], but it also varies in individual fields.

Previous studies had proved that TAF1/TAF1L played important roles in different kinds of tumor progression [8–10]. There were also several studies mentioned the potential role of TAF1/TAF1L in GC [8, 11, 12]. Until now, there was no study explored the relationship of TAF1L expression with clinicopathological features and prognosis of GC.

In this study, we evaluated the expression of TAF1L in clinical samples by immunohistochemistry and aims to investigate the clinical significance of TAF1L in GC and to explore a new potential biomarker for evaluating treatment and prognosis.

Materials and methods

Patient inclusion

In this study, we screened patients with inclusion and exclusion criteria. Therefore, 120 patients met the inclusion criteria, as well as 30 paired para-cancerous/normal samples of the enrollment.

Inclusion criteria: (1) histologically confirmed gastric or oesophagogastric junction adenocarcinoma; (2) receive surgical treatment as initial treatment; (3) age 18–80 years; (4) Eastern Cooperative Oncology Group performance status (ECOG) 0–1 [13]; and (5) complete clinicopathologic data. Exclusion criteria: (1) with distant metastasis; (2) previous anti-tumor therapy such as chemotherapy and radiotherapy; (3) combined with other malignancies; and (4) missing data.

Immunohistochemistry

Immunohistochemistry (IHC) was carried out according to the manufacturer's instructions (Leica Bond III, Germany). Four-micrometer-thick tissue sections were incubated with the primary rabbit anti-TAF1L antibody (1:250; 55170-1-AP, Proteintech, USA) for 15 min followed by the incubation with the secondary antibody for 8 min, DAB color development for 10 min.

All IHC results were interpreted by two independent pathologists blinded to this study. In case of disagreement between the two pathologists, the result would be re-evaluated by a third one. The degrees of staining intensity were determined as: 0 (none), 1 (weak), 2 (moderate),3 (intense) and 4 (strongly intense). Percentages of positive cell were counted as 0 (0%), 1 (1–25%), 2 (26–50%), 3 (51–75%) and 4 (76–100%). The final staining score was calculated by multiplying the intensity of the positive signal by the percentage of positive cells, following the method of Remmele and Stegner (1987) [14]. A score of <4 was considered as "low expression" and a score ≥ 4 as "high expression", and the categories were used for statistical analysis. To ascertain the mismatch repair (MMR) status, postoperative immunohistochemical analysis was conducted on four key MMR proteins: MLH1 (using Dako's ES05 clone), MSH2 (with Dako's FE11 clone), MSH6 (employing Dako's EP49 clone), and PMS2 (via Dako's EP51 clone). Loss of any of the four MMR proteins was defined as MMR deficiency (dMMR).

Follow-up

For enrolled patients, follow-up was performed once per 3 months in first 2 years, once per 6 months in 3 to 5 years and once yearly thereafter. The follow-up methods mainly included telephonic follow-ups and regular outpatient reexaminations. Overall survival (OS) was defined as the time from the date of pathological diagnosis of GC to the date of death or the most recent follow-up. The cutoff date for OS was December 31, 2023.

Bioinformatics analysis

TCGA dataset (https://tcgadata.nci.nih.gov/tcga) was used to gain the RNA-sequencing expression (level 3) profiles and clinicopathological information for stomach adenocarcinoma (STAD) cases. The differences in survival between the groups were compared by Log-rank test. The predictive accuracy of TAF1L mRNA was compared by the timeROC (v 0.4) analysis. R software package ggstatsplot and pheatmap were used to display the two-gene correlation map and the multi-gene correlation respectively. Spearman's correlation analysis was used to describe the correlation between quantitative variable that without a normal distribution. The Genomics Analysis and Visualization

Platform tool (http://r2.amc.nl) was used to preform KEGG (Kyoto Encyclopedia of Genes and Genomes) and GO (Gene Ontology) analyses.

Statistical analysis

SPSS 26.0 (IBM Corporation, Armonk, NY, USA) and R 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria) were used for statistical analyses and $p<0.05$ was indicated statistical significance. Student t-test or Chi-squared test was used to assess the between-group differences regarding to continuous or discrete variables, respectively. Survival analysis was performed by the Kaplan-Meier method with Log-rank test. Univariate and multivariate analyses based on Cox hazard regression models were used to evaluate the prognostic factors, Hazard ratio (HR) and 95% confidence interval (CI). Cox proportional hazards regression model was used for univariate and multivariate analysis to identify the risk factors affecting the survival status of patients and estimated hazard ratio (HR) and 95% confidence interval (95% CI).

Results

Baseline characteristics

In this study, a total of 1053 GC patients in Zhejiang Cancer Hospital (Hangzhou, China) between January 1st, 2018 to December 31th, 2019 were screened, while 479 patients had distant metastasis, 261 patients had received preoperative chemotherapy, 96 patients concurrent with other primary tumors, 47 patients were either under 18 or over 80 years old, 29 patients had incomplete clinicopathologic data and 21 patients were loss to follow-up. Finally, 120 patients met the inclusion criteria. 83 (69.2%) were male and 37 (30.8%) were female, and the median age was 59 years (range 26–80). All the patients received surgical treatment as initial treatment and postoperative pathology showed 72 cases (60.0%) were poorly/undifferentiated adenocarcinoma. The number of stages I, II, III cases was 15 (12.5%), 33(27.5%), 72(60.0%), respectively. The details of patient characteristics were shown in Table 1.

Clinicopathological features and immunohistochemical expression of TAF1L

TAF1L expression was evaluated by IHC in surgical specimens, and the results showed that TAF1L was higher expressed on the tumor tissues than para-cancerous/normal tissues. (Fig. 1a, expression of TAF1L in tumor tissue; Fig. 1b, expression of TAF1L in para-cancerous/normal tissue; Fig. 1c Representative image of TAF1L IHC staining by scoring). According to the results of IHC, there were 55 GC patients (45.8%) in the high-expression group (TAF1L-H group) while 65 GC patients (54.2%) in the low-expression group (TAF1L-L group).

TAF1L expressions were mainly correlated with tumor differentiation ($p=0.046$), signet-ring cells ($p=0.043$), dMMR status ($p=0.011$), lympho-vascular invasion ($p=0.038$) and neural invasion ($p=0.005$) as shown in Table 1.

Survival analysis

There was significant difference in OS between the TAF1L-H group and the TAF1L-L group (mean OS: 40.3 months vs. 51.8 months, $p=0.019$; Fig. 2). Furthermore, we analyzed the survival differences in subgroups according to the pathological features. The results showed that the TAF1L-H cases presented worse survival in HER2-positive GC (mean OS: 20.9 months vs. 51.2 months, $p=0.007$, Fig. 3a) while no statistical difference in HER2-negative GC (mean OS: 43.6 months vs. 51.1 months, $p=0.168$, Fig. 3b). As for mismatch repair (MMR) status, the survival of TAF1L-H group was significantly worse than that of TAF1L-L group in mismatch repair-proficient (pMMR) cases (mean OS: 38.8 months vs. 51.6 months, $p=0.006$, Fig. 3c) but not in mismatch repair-deficient (dMMR) cases ($p=0.724$, Fig. 3d). Besides, TAF1L-H cases showed worse OS both in stage I/II diseases and stage III diseases compared to TAF1L-L cases, although there were no statistical differences ($p=0.075$ and 0.119, respectively).

Prognostic factors analysis

Univariate Cox regression showed that the expressions of TAF1L, tumor size, N stage, HER2 status were statistically significant as the prognostic risk factors. Multivariate analysis showed that the expression of TAF1L (HR=2.044, 95%CI=1.007–4.147, $p=0.048$) and HER2 status (HR=2.383, 95%CI=1.087–5.222, $p=0.030$) were independent prognostic risk factors (Table 2).

Moreover, in HER2-positive cases ($n=18$), TAF1L was the independent prognostic risk factor (HR=6.736, 95%CI=1.373–33.032, $p=0.019$). In HER2-negative cases ($n=102$), however, TAF1L showed no significant relationship with the prognosis (HR=1.718, 95%CI=0.789–3.741, $p=0.173$). Besides, HER2 status was also the independent prognostic risk factor in TAF1L-H group (HR=4.832, 95%CI=1.908–12.239, $p=0.001$), but not in TAF1L-L group (HR=1.023, 95%CI=0.227–4.616, $p=0.977$). Due to the limited case number, we were unable to analyze the role of TAF1L in the prognosis of dMMR cases. In the pMMR cases, TAF1L was also the independent prognostic risk factor (HR=2.291, 95%CI=1.126–4.660, $p=0.022$).

Table 1 Baseline characteristics of 120 GC patients

Variable	TAF1L-H Group ($n=55$)	%	TAF1L-L Group ($n=65$)	%	χ2-value	*p*-value
Age (years)						
Median (min - max)	61.0 (31.0–80.0)		57.0 (26.0–79.0)			
Mean ± SD	61.2 ± 9.73		57.4 ± 11.93			
BMI						
Mean ± SD	22.2 ± 3.23		22.9 ± 2.87			
Sex					1.377	0.165
Male	41	74.5	42	64.6		
Female	14	25.5	23	35.4		
Smoking history					0.767	0.381
Yes	22	40.0	21	32.3		
No	33	60.0	44	67.7		
Drinking history					0.255	0.613
Yes	14	25.5	14	21.5		
No	41	74.5	51	78.5		
Tumor Size (cm)					2.303	0.091
< 5	28	50.9	42	64.6		
≥ 5	27	49.1	23	35.4		
pT-stage					0.060	0.491
≤T2	12	21.8	13	20.0		
> T2	43	78.2	52	80.0		
pN-stage					2.762	0.070
N0/1	18	32.7	31	47.7		
N2/3	37	67.3	34	52.3		
Tumor location					1.612	0.447
Upper	8	14.5	11	16.9		
Middle	9	16.4	16	24.6		
Lower	38	69.1	38	58.5		
Differentiation					3.497	0.046
Poorly/undifferentiated	38	69.1	34	52.3		
Well/moderately	17	30.9	31	47.7		
Signet-ring cells					3.689	0.043
Negative	47	85.5	46	70.8		
Positive	8	14.5	19	29.2		
Serum CEA (ng/mL)					0.377	0.373
Normal	48	87.3	59	90.8		
> 5	7	12.7	6	9.2		
Serum CA199 (U/mL)					2.718	0.077
Normal	48	87.3	49	75.4		
> 37	7	12.7	16	24.6		
Serum CA125 (U/mL)					0.999	0.212
Normal	41	74.5	43	66.2		
> 35	14	25.5	22	33.8		
MMR status					7.265	0.011
pMMR	47	85.5	64	98.5		
dMMR	8	14.5	1	1.5		
HER2					0.016	0.553
Negative	47	85.5	55	84.6		
Positive	8	14.5	10	15.4		
Ki-67					1.958	0.115
< 50% positive	13	23.6	23	35.4		
≥ 50% positive	42	76.4	42	64.6		
LVI					3.812	0.038
Negative	19	34.5	34	52.3		

Table 1 (continued)

Variable	TAF1L-H Group ($n=55$)	%	TAF1L-L Group ($n=65$)	%	χ2-value	*p*-value
Positive	36	65.5	31	47.7		
NI					7.762	0.005
Negative	27	49.1	49	75.4		
Positive	28	50.9	16	24.6		

CEA: Carcinoembryonic antigen; CA199: Carbohydrate antigen199; CA125: Carbohydrate antigen 125; LVI: Lympho-vascular invasion; NI: Nerve invasion

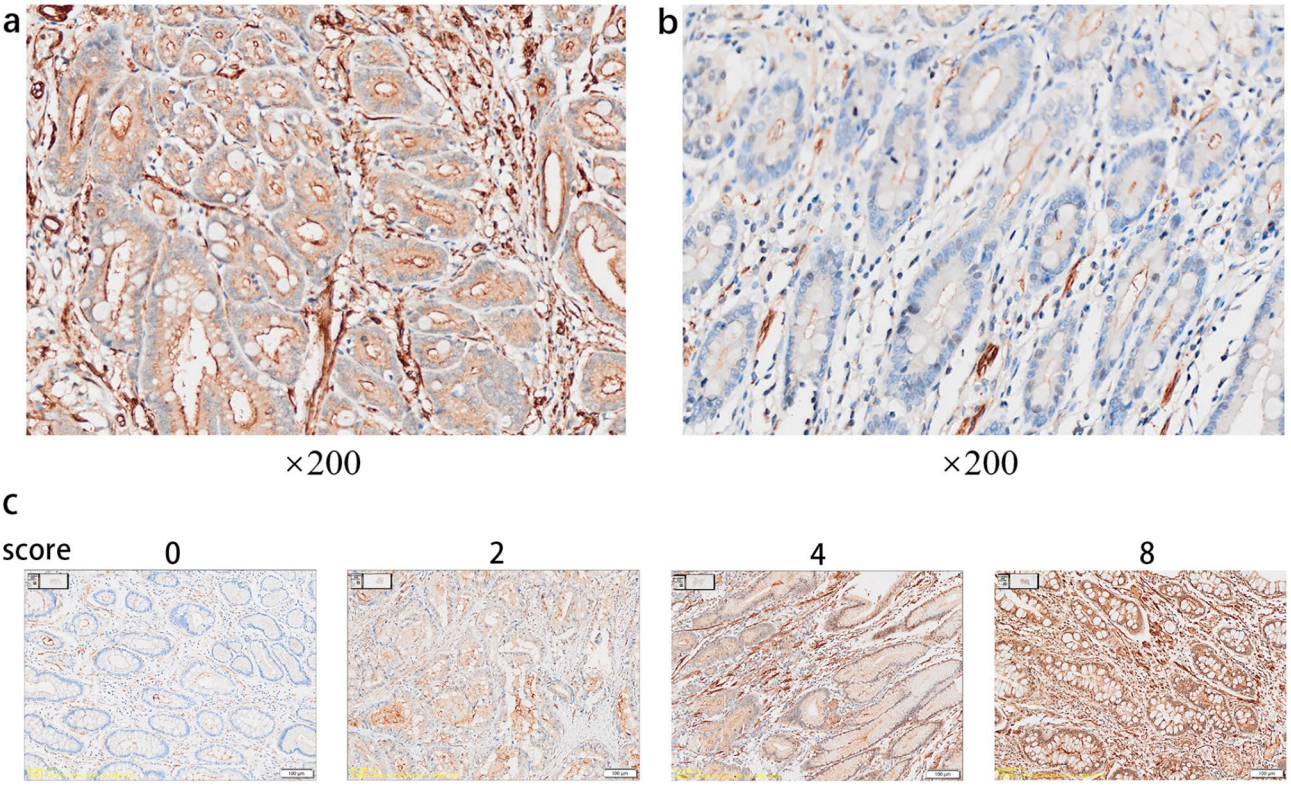

Fig. 1 Representative TAF1L immunohistochemical staining images. **a** Expression of TAF1L in tumor tissue; **b** Expression of TAF1L in para-cancerous/normal tissue; **c** Representative image of TAF1L IHC staining by scoring

Bioinformatics analysis of TAF1L

As TCGA-GC dataset results showed, the expression of TAF1L was significantly higher in tumors compared with the normal control tissues ($p<0.001$, Fig. 4a). Additionally, we further analyzed the relationship between TAF1L and some classical biomarkers associated with treatment. According to the results, TAF1L presented lower expression in microsatellite instability-high (MSI-H) GC than microsatellite-stable (MSS) GC ($p=0.002$). Moreover, we analyzed the expression relationship between TAF1L and the main four DNA mismatch repair (MMR) protein genes (MLH1, MSH2, MSH6, PMS2), and the results presented significant positive correlations ($p<0.01$). As for HER2 status, the gene correlation analysis suggested a significant correlation between ERBB2 (HER2) and TAF1L ($p=0.002$). Compared with HER2-negative cases, HER2-positive cases presented higher TAF1L expression ($p=0.005$).

Survival analysis found that high expression of TAF1L cases showed worse OS which presented significant difference ($p<0.001$, Fig. 4b). Further analysis showed that TAF1L high expression tended to have worse survival both in MSI-H group (34.0 months vs. *NE*, $p=0.054$, Fig. 5a) and MSS group (11.0 months vs. 35.0 months, $p=0.0046$, Fig. 5b). In HER2-positive cases, TAF1L expression was negatively correlated with OS (24.0 months vs. 57.0 months, $p=0.0039$, Fig. 5c), while no significant difference in HER2-negative ones (30.0 months vs. 39.0 months, $p=0.16$, Fig. 5d).

KEGG analysis revealed the genes showed highly correlation with TAF1L were mainly focused on biological processes such as p53 signaling pathway, mismatch repair, IL-17 signaling pathway, and cell cycle (Fig. 6a). GO analysis showed that the biological functions of TAF1L and its related genes mainly

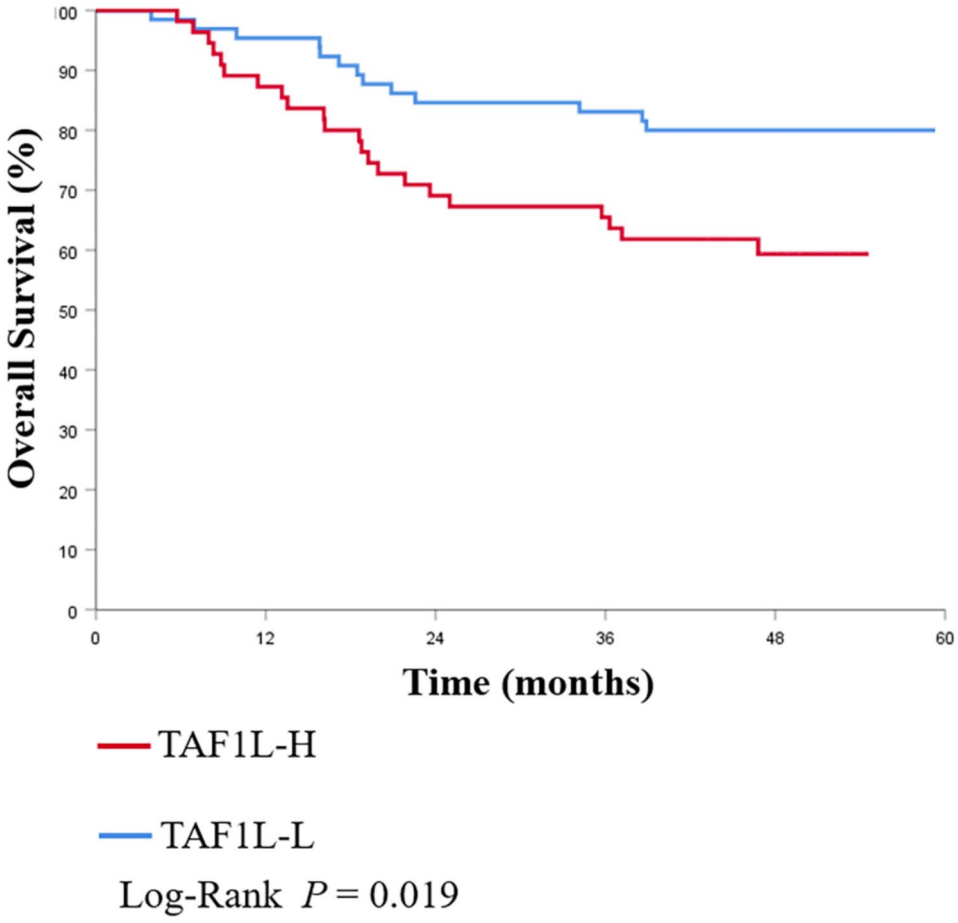

Fig. 2 Kaplan-Meier analysis of overall survival according to the expression of TAF1L in the whole cohort ($p = 0.019$)

concentrated in biological processes such as organelle fission, cell cycle checkpoint, nuclear division, and DNA replication (Fig. 6b). These biological behaviors may participate in GC occurrence and progression.

Discussion

GC is characterized by high heterogeneity and a comprehensive molecular profile can greatly facilitate the evolution of treatment regimens and the improvement of precision in population selection. Researching GC biomarkers is of great significance to improve the treatment efficacy and prognosis.

TAF1L was first found to present high expression in human testicular germ cells by P. Jeremy et al., and its similarity to TAF1 was greater than 94% [15], which mainly played a role in transcriptional regulation and histone acetyltransferase activity [4, 6, 7]. Currently, only several studies revealed the potential role of TAF1/TAF1L in the occurrence and development of GC [8, 11, 12]. However, its relationship with prognosis and clinicopathological features in GC remains unclear. Thus, this study aims to evaluate the probability of TAF1L as a new potential biomarker of treatment and prognosis evaluation in GC.

In this study, we performed IHC to evaluate the TAF1L expression in GC tissues. According to IHC staining results, TAF1L expression in GC tissue sections was much stronger than those in normal/paracancerous ones. Moreover, the expression of TAF1L were correlated with tumor differentiation, signet-ring cells, dMMR status, lympho-vascular invasion, and neural invasion in this cohort, which suggested that TAF1L is closely related to the occurrence and development of GC. Survival analysis showed that high expression of TAF1L presented worse survival, and the result of TCGA dataset also showed similar tendency. Besides, the multivariate analysis suggested the expression of TAF1L is one of the independent prognostic risk factors. These results revealed that the expression of TAF1L is related to the progression of GC and may act as a potential prognosis biomarker of GC.

Previous study showed that TAF1 and TAF1L genes had mononucleotide repeats in the coding sequences that might be mutation targets in the cancers with MSI [8], which may promoting the tumorigenesis of MSI-H

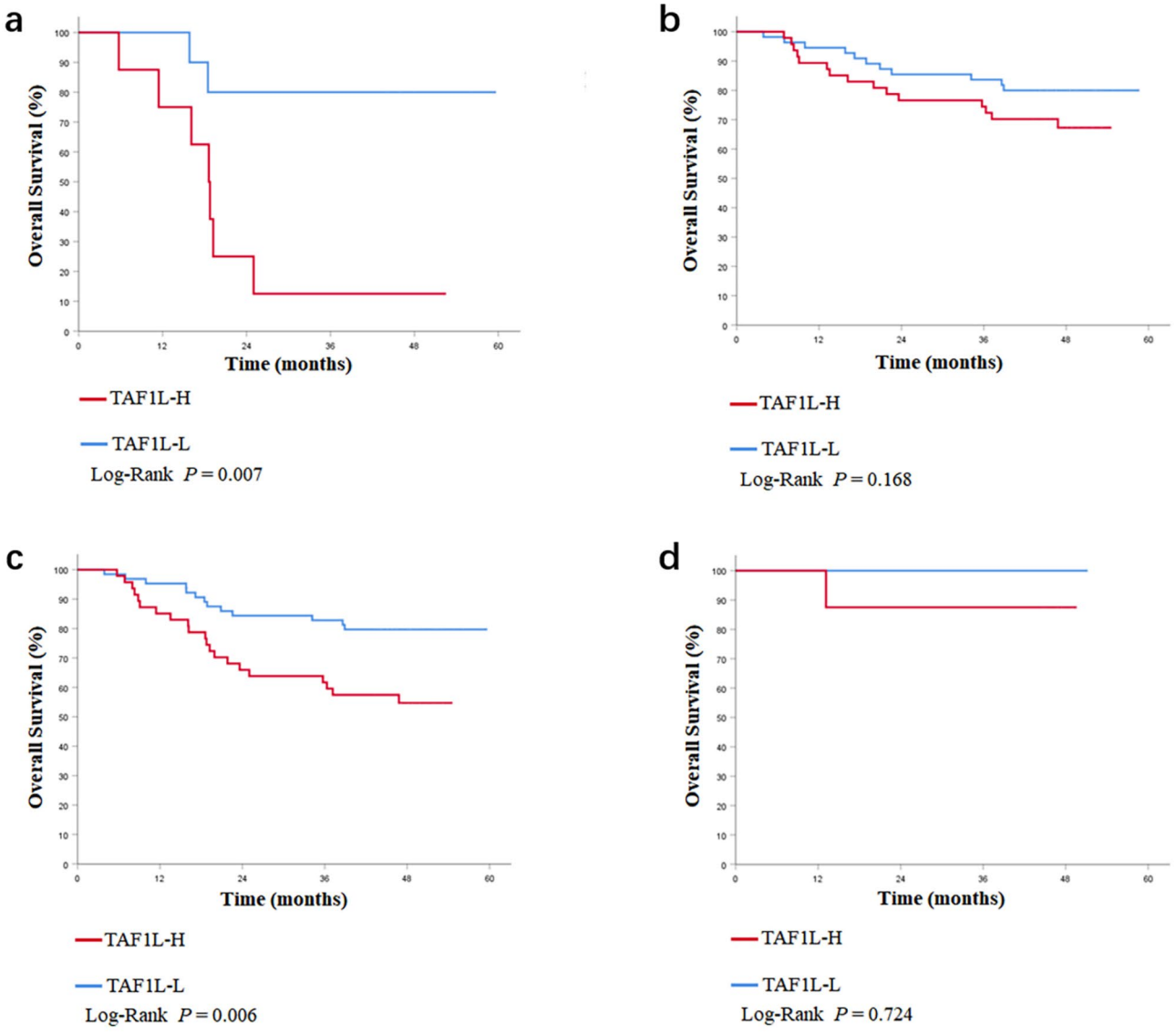

Fig. 3 Kaplan-Meier analysis of overall survival according to the expression of TAF1L in clinical samples. **a** HER2-positive cases ($p = 0.007$); **b** HER2-negative cases ($p = 0.168$); **c** pMMR cases ($p = 0.006$); **d** dMMR cases ($p = 0.724$)

GC. MMR is critical for genome stability and dMMR can result in MSI phenotype [16], and the concordance between MSI-H status and dMMR was 97.6–99% [17, 18]. In our cohort, the TAF1L-H group presented higher dMMR proportion (14.5%, 8/55) than TAF1L-L group (1.5%, 1/65) and there was statistical difference ($p = 0.011$). As the prevalence of dMMR/MSI-H was 6-10% in eastern cohorts [19–21], our results suggested that the higher expression of TAF1L may presented more frequency of dMMR status. However, the frameshift mutations would result in premature stops of amino acid synthesis in TAF1L protein [8], indicating that low expression of TAF1L is associated with MSI-H/dMMR status, which is contrary to our results. Thus, we further explore the relationship between TAF1L and MSI-H/dMMR status.

According to the TCGA dataset, TAF1L presented lower expression in MSI-H cases ($p = 0.00413$). Moreover, TAF1L presented significant positive correlations with MLH1, MSH2, MSH6 and PMS2 expression, suggesting that low expression of TAF1L might cause the deficiency of MMR protein expression and resulting in dMMR status. Although our conclusion was not consistent with the TCGA results due to the rarity of dMMR GC and the limited cases of our cohort, the expression of TAF1L did correlate with MSI-H/dMMR status and was expected to be confirmed by larger sample size studies in the future.

Table 2 Univariate and multivariate analysis of prognostic factors for OS

Variable	Univariate		Multivariate	
	HR (95%CI)	*p*-value	HR (95%CI)	*p*-value
Age (≥ 50 years)	1.316 (0.677–2.560)	0.418		
Sex (Male)	0.950 (0.465–1.940)	0.888		
TAF1L Exprssion (High)	2.274 (1.145–4.516)	0.019	2.044 (1.007–4.147)	0.048
Tumor Size (≥ 5 cm)	2.328 (1.183–4.582)	0.014	1.870 (0.922–3.791)	0.083
T-stage (> T2)	2.316 (0.817–6.566)	0.114		
N-stage (N2-3)	2.214 (1.037–4.727)	0.040	1.465 (0.656–3.274)	0.352
Differentiation (Poorly/undifferentiated)	1.183 (0.596–2.348)	0.631		
Signet-ring cells	1.563 (0.750–3.254)	0.233		
MMR status (dMMR)	0.541 (0.074–3.949)	0.544		
HER2	2.425 (1.133–5.191)	0.023	2.383 (1.087–5.222)	0.030
Ki-67 (≥ 50% positive)	1.122 (0.550–2.291)	0.751		
LVI	1.696 (0.844–3.410)	0.138		
NI	1.297 (0.635–2.648)	0.476		
CEA (> 5 ng/mL)	1.755 (0.728–4.231)	0.210		
CA199 (> 37 U/mL)	1.648 (0.791–3.432)	0.182		
CA125 (> 35 U/mL)	1.514 (0.762–3.007)	0.237		

CEA: Carcinoembryonic antigen; CA199: Carbohydrate antigen199; CA125: Carbohydrate antigen 125; LVI: Lympho-vascular invasion; NI: Nerve invasion

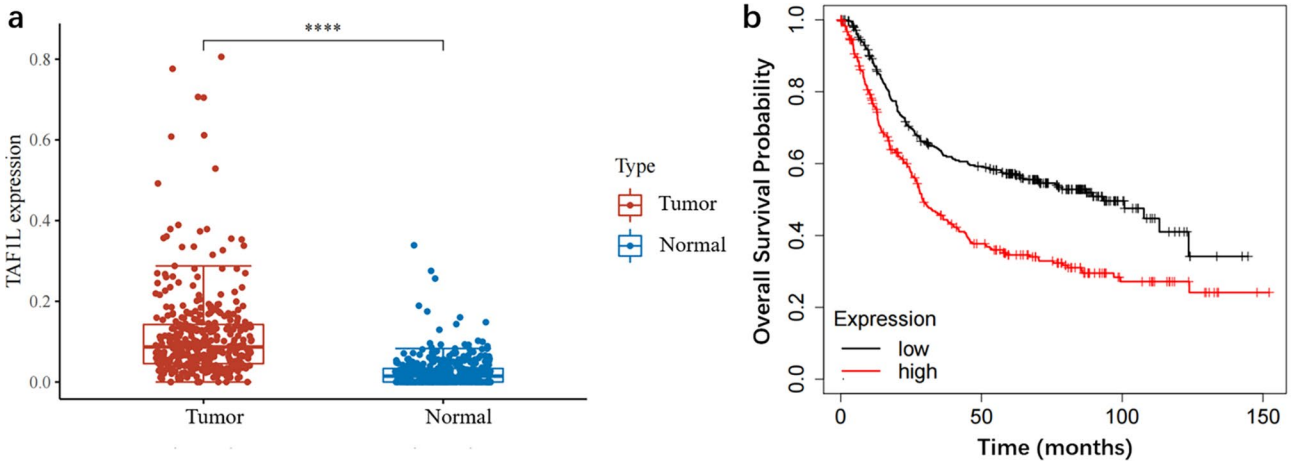

Fig. 4 The mRNA expression level of TAF1L in the TCGA GC dataset. **a** TAF1L expression in tumors is higher than that in normal tissues (**** $p < 0.001$); **b** Kaplan-Meier analysis of overall survival according to the expression of TAF1L in the TCGA GC dataset ($p < 0.001$)

Through whole-genome sequencing, Zhou et al. found that TAF1 was an important mutated driver gene in HER2-positive GC [12]. Moreover, Cai et al. found that the co-expression of TAF1 and HER2 cases presented worse prognosis in endometrial clear cell carcinoma [22]. These results indicated the potential relationship of TAF1 and HER2 in cancer progression. As TAF1L is an analogue of TAF1, we further analyzed the correlation of TAF1L and HER2 in GC. Survival analysis based on TCGA dataset showed that TAF1L expression was negatively correlated with OS in HER2-positive GC samples ($p = 0.0039$), but not in HER2-negative ones ($p = 0.16$). Moreover, the gene correlation also suggested a significant association between ERBB2 and TAF1L ($p = 0.002$).

In our cohort, the TAF1L-H cases showed worse survival in HER2-positive GC ($p = 0.007$) and TAF1L was the independent prognostic risk factor in HER2 positive cases. However, there was no relationship between TAF1L expression and HER2 status ($p = 0.553$) in this cohort, which may be caused by the limited case number. In conclusion, TAF1L might play an important role in HER2-positive GC progression and the co-expression of TAF1L and HER2 in GC may results in worse prognosis. Further studies are expected to explore the relationship and mechanisms of interaction between TAF1L and HER2 status in GC.

As studies reported previously, immune-checkpoint inhibitors (ICIs) in dMMR/MSI-H GC had been well validated in several phase II and III studies [23–25].

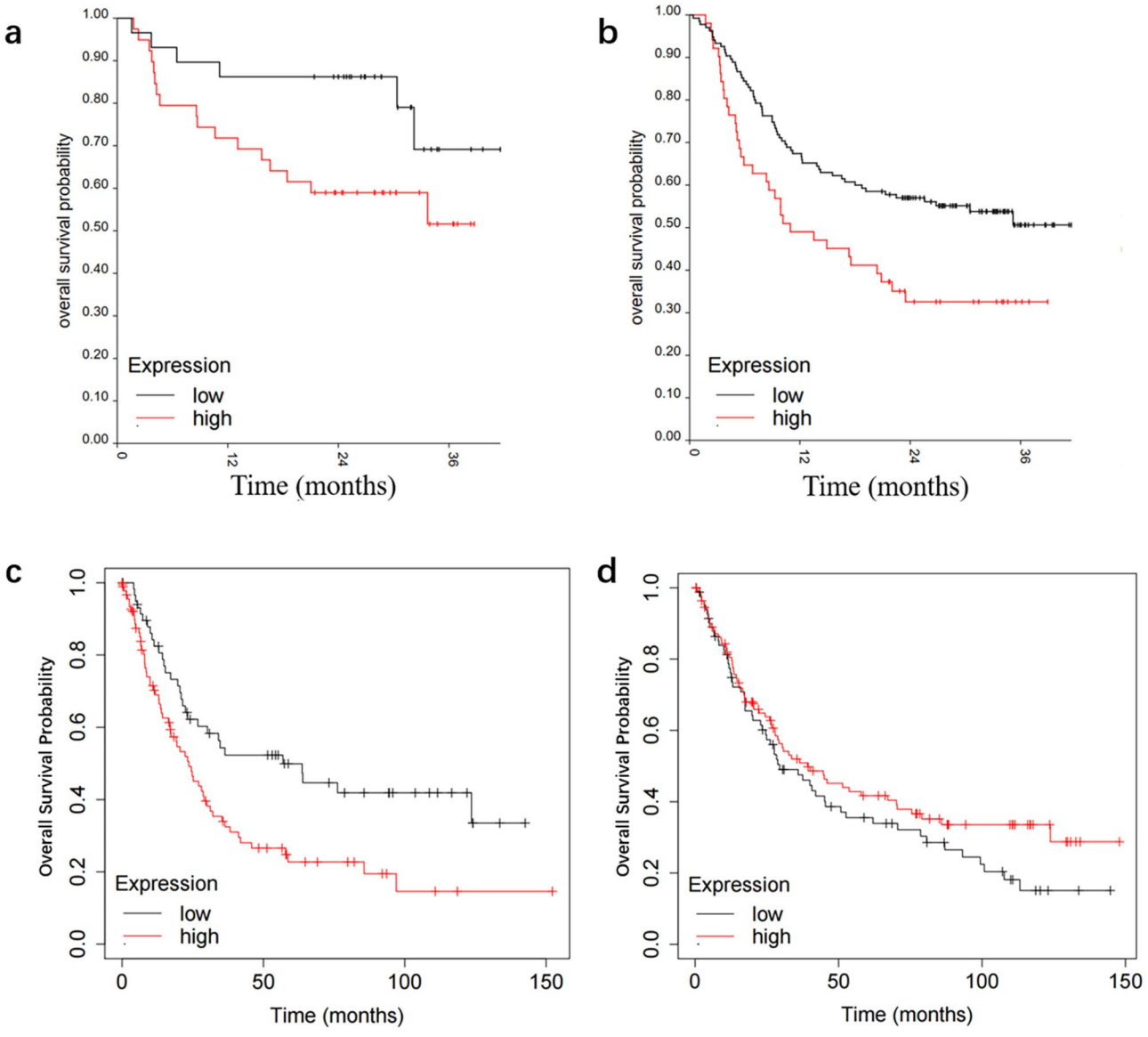

Fig. 5 Kaplan-Meier analysis of overall survival according to the expression of TAF1L in different TCGA dataset. **a** MSI-H GC dataset ($p = 0.054$); **b** MSS GC dataset ($p = 0.0046$); **c** HER2-positive GC dataset ($p = 0.0039$); **d** HER2-negative GC dataset ($p = 0.16$)

According to our KEGG analyze results, IL-17 signaling pathway was one of the top-20 enriched pathways related to TAF1L. Several studies had indicated the importance of IL-17 in cancer immunotherapy which involved in tumor microenvironment [26–28]. Targeting the IL-17/TAF1L immune axis may become a new way improving immunotherapy efficacy. Moreover, targeted therapy such as trastuzumab has been wildly used in HER2-positive GC [29, 30]. As our results revealed the relationships between TAF1L together with MSI-H/dMMR and HER2 status, indicating that TAF1L may be associated with immunotherapy and targeted therapy efficacy. However, these were only inferences based on our results and did not conduct further analysis because of the limited cases. The correlation between TAF1L and the efficacy of different treatment regimens needs to be further studied.

Our study also had some limitations. First, it was retrospective study in a single-center as the overall sample size was relatively small, and large-sample studies might be necessary to clarify our result. Second, although we performed preliminary IHC to evaluate the expression of TAF1L in clinical samples and validated by TCGA dataset, some results still need to be validated by wet-experiment and we would like to conduct in future study. In addition, because most of the surgical specimens of stage IV patients were after treatment (such as chemotherapy or immunotherapy), we did not include such patients for analysis, and we expected further studies to discuss the role of TAF1L

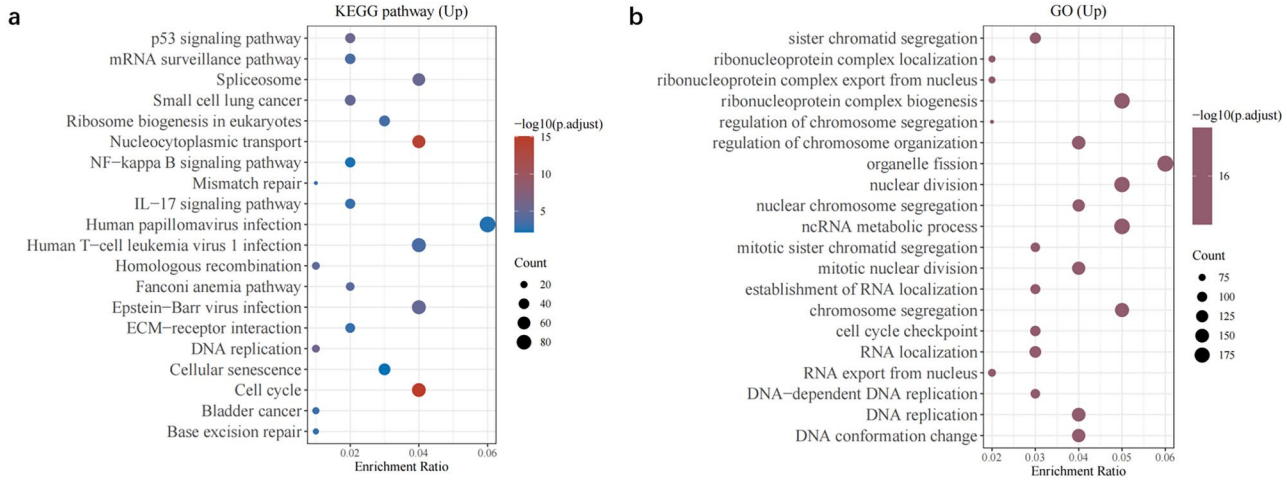

Fig. 6 Functional enrichment of TAF1L in the TCGA GC dataset. **a** KEGG enrichment analysis of pathways associated with TAF1L in the TCGA GC dataset; **b** GO enrichment analysis of pathways associated with TAF1L in the TCGA GC dataset

in such patients in the future. Despite these, as far as we know, it is the first study focusing on TAF1L expression and revealing its potential relationship with clinicopathological features of GC, which is important for future exploration of new biomarker in therapy and prognosis.

In conclusion, TAF1L presents high expression in GC tissues and is closely related to the occurrence and development of GC. Moreover, high expression of TAF1L is a marker of poor prognosis, especially in HER2 positive GC cases. We suppose that TAF1L might become a significant biomarker for predicting prognosis as well as a potential therapeutic biomarker in GC. However, further in vitro and in vivo experiments were needed to explore the mechanism of TAF1L acting on GC tumor progression. Overall, our findings provide a basis for understanding the function of TAF1L in GC, which will provide theoretical basis and new ideas for the target of gene detection, diagnosis, and treatment in the future.

Author contributions

Han Chen, Hang Chen, JF and PY designed the study. Han Chen, JF, XH, and TC analyzed the data. Han Chen and JF drafted the manuscript. Hang Chen, XZ and LH collected and registered the data. PY, XC and LH interpreted the data and revised the manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by Zhejiang Cancer Hospital Ethics Committee (No. IRB-2022-691). Human Ethics and Consent to Participate declarations: not applicable. Informed consent was waived by the Ethics Committee of the Zhejiang Cancer Hospital because of the retrospective study of this project.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

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