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Bioinformatic Analysis and Experimental Verification Reveals KBTBD6 as a Novel Prognostic Genes Associated with Immune Infiltration in OSCC

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Abstract: Oral squamous cell carcinoma (OSCC) is one of the most common malignant tumors and has a poor prognosis. Kelch repeat and BTB domain-containing protein 6 (KBTBD6) regulates the cytoskeleton, cell proliferation, and cell migration as part of the CUL3 (KBTBD6/7) E3 ubiquitin ligase complex, and has been associated with the development of pituitary adenomas. Here, a bioinformatics analysis was conducted using data from OSCC patients in The Cancer Genome Atlas database. Results indicate that KBTBD6 levels in OSCC patient tissues were significantly higher than in normal tissues. Additionally, high KBTBD6 expression correlated with poor prognosis. Functional annotation of differentially expressed genes associated with KBTBD6 in the OSCC cohort revealed significant enrichment of the interleukin-17 signaling pathway. Furthermore, KBTBD6 expression also correlated significantly with immune cell subset infiltration and immune checkpoint gene expression. These findings suggest that KBTBD6 is a promising therapeutic target and prognostic indicator in OSCC.

Keywords: KBTBD6; OSCC; Immune; Immune checkpoint; Prognosis

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1. Introduction

Oral squamous cell carcinoma (OSCC) is one of the most common types of head and neck squamous cell carcinoma (HNSC) and is associated with a relatively poor prognosis [1,2]. Due to the rich blood flow and the presence of numerous lymph nodes in the oral cavity, OSCC cells proliferate and metastasize rapidly [3]. Despite advances in treatment strategies such as radiotherapy, chemotherapy, and surgery, global OSCC patient mortality rates remain high, with survival rates below 50% [4,5]. Understanding the mechanisms underlying

OSCC progression is therefore essential to developing more effective targeted therapies.

Kelch repeat and BTB structural domain-containing protein 6 (KBTBD6) belongs to the BTB-Kelch protein family, associated with antigen processing and presentation mediated by class I major histocompatibility complex (MHC) and protein metabolism, and is closely related to KBTBD7. KBTBD6/7 regulates Rac family small GTPase 1 (RAC1) signaling and its downstream biological processes, such as cytoskeleton modeling, proliferation, and migration, through ubiquitination [6]. The BTB-Kelch protein family has strong associations with various tumors; for instance, KBTBD7 promotes lung cancer development by mediating phosphatase and tensin homolog (PTEN) ubiquitination [7], KBTBD1 is linked to poor prognosis and immunosuppression in hepatocellular carcinoma [8], and KBTBD8 can inhibit epithelial ovarian cancer progression [9]. In colon adenocarcinoma, KBTBD11 has been shown to influence prognosis and recurrence [10]. However, the role of KBTBD6 in tumors remains largely unknown.

This study identifies abnormal KBTBD6 expression across multiple tumor types, with strong associations to prognosis and immune infiltration. Specific mechanisms of KBTBD6 in OSCC were investigated through KBTBD6-related gene analysis, including assessments of its impact on conventional chemotherapeutic agent sensitivity. This research advances the understanding of OSCC treatment and diagnosis, positioning KBTBD6 as a potential target for immunotherapy and drug therapy.

2. Materials and methods

2.1. Pan-cancer analysis

The expression of the *KBTBD6* gene was analyzed using the TIMER2.0 database (http://timer.cistrome.org/) and pan-cancer data from The Cancer Genome Atlas (TCGA) and the combined Genotype-Tissue Expression (GTEx) database [11]. A total of 11,123 samples and related clinical data were downloaded from TCGA. The survival package was used to conduct pan-cancer proportional hazards hypothesis testing and perform Cox regression analysis [12]. Furthermore, the ssGSEA algorithm provided in the R package GSVA was used to calculate immune infiltration status across pan-cancer data [13].

2.2. Survival analysis

After excluding cases with missing clinical information, OSCC cases were divided into KBTBD6^{high} and KBTBD6^{low} groups based on the median KBTBD6 expression level. Proportional hazards hypothesis testing was conducted using the survival package, followed by fitted survival regression. The “survminer” package and the “ggplot2” package were used to visualize the Kaplan-Meier curve.

2.3. Receiver operating characteristic curve

The receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive efficacy of KBTBD6 for OSCC patients, using the R package “pROC.”

2.4. Co-expression analysis

The “limma” package in R software was used to screen genes co-expressed with *KBTBD6* from the transcriptome data of the TCGA-OSCC cohort, and these genes were visualized. Correlation coefficients were calculated using Pearson’s method, with significance set at $P < 0.001$.

2.5. Protein-protein interaction network system

To further explore protein interaction relationships, 22 genes associated with *KBTBD6* were uploaded to the GENEMANIA database to construct a KBTBD6-related protein-protein interaction network. The gene screening threshold was set at a correlation coefficient > 0.6 and $P < 0.001$ [14].

2.6. Identification of KBTBD6-related genes

To identify genes closely related to *KBTBD6*, OSCC patients were divided into $KBTBD6^{high}$ and $KBTBD6^{low}$ groups. The "limma" package was applied to screen differentially expressed genes with criteria of |logFC| > 1 and $P < 0.05$, and these genes were visualized in a heatmap.

2.7. Functional enrichment analysis

To understand the role of KBTBD6 in OSCC, the "clusterProfiler" R package was used to perform Kyoto Encyclopedia of Genes and Genomes (KEGG) and Gene Ontology (GO) analyses on *KBTBD6*-related differentially expressed genes.

2.8. Immune infiltration analysis

The immune cell infiltration score of quantified samples was calculated using the CIBERSORT algorithm. Correlation calculations were performed using the Spearman method, with the significance threshold set at $P < 0.05$.

2.9. Immune checkpoint analysis

The correlation of *KBTBD6* with 47 immune checkpoint-associated genes was determined using Pearson correlation analysis, with the *P*-value threshold set at < 0.001.

2.10. Drug sensitivity

The "pRRophetic" R package was used to analyze IC_{50} values for chemotherapeutic drugs in the TCGA-OSCC cohort. The Wilcoxon test was applied to compare IC_{50} values between the $KBTBD6^{high}$ and $KBTBD6^{low}$ groups.

2.11. Single-cell assay

Single-cell data (GSE172577) from the Tumor Immune Single-Cell Hub (TISCH2) database were analyzed to determine the distribution of KBTBD6 at the single-cell level. Cell clusters were annotated and visualized by the uniform manifold approximation and projection method (UMAP) [15].

2.12. Tissue microarray analysis

Processing and analysis of the tissue microarray were conducted by Xi'an Biotechnology Co. Ltd. in China. The acquisition number for the tissue microarray is HN054Oc01. KBTBD6 levels in 45 tongue cancer specimens and 9 adjacent tongue tissues were detected by immunohistochemistry [16].

2.13. Cell culture

Human tongue cancer cell lines SCC9 and SCC25 were obtained from BNCC. SCC9 cells were cultured in DMEM containing 10% fetal bovine serum (FBS), 100 μg/mL penicillin, and streptomycin, while SCC25 cells

were cultured in DMEM-H/F-12K containing 10% FBS and 400 ng/mL hydrocortisone. Cells were maintained in a humidified incubator at 37°C with 5% CO_2.

2.14. RT-qPCR

Total RNA from treated cells was extracted using the RNeasy Mini Kit (Qiagen, 74104). cDNA was synthesized using the RT Master Mix kit (MedChemExpress, HY-K0511), and qPCR detection was performed on the Applied Biosystems 7500 FAST Real-Time PCR system using SYBR Green qPCR Master Mix (MedChemExpress, HYK0522). Primer sequences for the experiment were as follows:

ACTB forward 5′-CACCATTGGCAATGAGCGGTTC-3′, reverse 5′-AGGTCTTTGCGGATGTCCACGT-3′.

KBTBD6 forward 5′-AACAGCAGCAGCAGCAGTAGC-3′, reverse 5′-CACCATCTCCTTGGCACACATACC-3′.

2.15. Cell transfection

KBTBD6 siRNA was purchased from GenePharma Co., Ltd. and transfected into cells using GP-transfect-Mate (GenePharma) as per the supplier's instructions. The siRNA sequences used in the experiment were as follows:

Control siRNA 5′-GCTTCGCGCCGTAGTCTTATCA-3′, KBTBD6 siRNA 5′-CCUUUACAAAGUGCCGUCATT-3′.

2.16. Cell viability assay

Transfected cells were cultured for 0, 24, 48, and 72 hours. The cell counting kit-8 (CCK-8, MedChemExpress HK-K0301) was applied according to the manufacturer's instructions. A multimode plate reader (Molecular Devices) was used to measure absorbance at 450 nm, and results were processed.

2.17. Statistical analysis

All statistical analyses were performed using R (v4.3.2, R Foundation for Statistical Computing) and GraphPad Prism (version 8.00, GraphPad Software Inc.). A P-value <0.05 was considered statistically significant.

3. Results

3.1. KBTBD6 is abnormally expressed and associated with prognosis and immunity in cancers

The TIMER database was used to compare KBTBD6 expression across 33 tumors and normal tissues. KBTBD6 expression was significantly different in breast cancer (BRCA), cholangiocarcinoma (CHOL), colon adenocarcinoma (COAD), glioblastoma multiforme (GBM), esophageal carcinoma (ESCA), head and neck squamous cell carcinoma (HNSC), kidney renal papillary cell carcinoma (KIRP), kidney chromophobe (KICH), kidney renal clear cell carcinoma (KIRC), liver hepatocellular carcinoma (LIHC), pheochromocytoma and paraganglioma (PCPG), lung squamous cell carcinoma (LUSC), rectum adenocarcinoma (READ), skin cutaneous melanoma (SKCM), uterine corpus endometrial carcinoma (UCEC), stomach adenocarcinoma (STAD), and thyroid carcinoma (THCA) (**Figure 1a**). To further analyze expression differences, TCGA data combined with the GTEx database was utilized. Results showed increased expression of KBTBD6 in adrenocortical carcinoma (ACC), BRCA, COAD, diffuse large B-cell lymphoma (DLBC), ESCA, HNSC, KICH, low-grade glioma (LGG), pancreatic adenocarcinoma (PAAD), STAD, and SKCM (**Figure 1b**).

To assess the potential impact of KBTBD6 expression on tumor prognosis, Cox regression survival analysis was conducted in the TCGA cohort. Statistical significance was observed in HNSC, KIRC, and

LGG. Specifically, in HNSC, the hazard ratio (HR) was greater than 1 (95% CI: 1.039–1.785), suggesting that KBTBD6 may act as a risk factor in HNSC (**Figure 1c**). Immune infiltration for 24 immune cell types in the TCGA cohort was calculated using the ssGSEA algorithm, revealing a significant correlation of KBTBD6 with multiple immune cells, including T cells, natural killer (NK) cells, and B cells across various tumor types. These results suggest that KBTBD6 may have an influential role in the tumor microenvironment (**Figure 1d**).

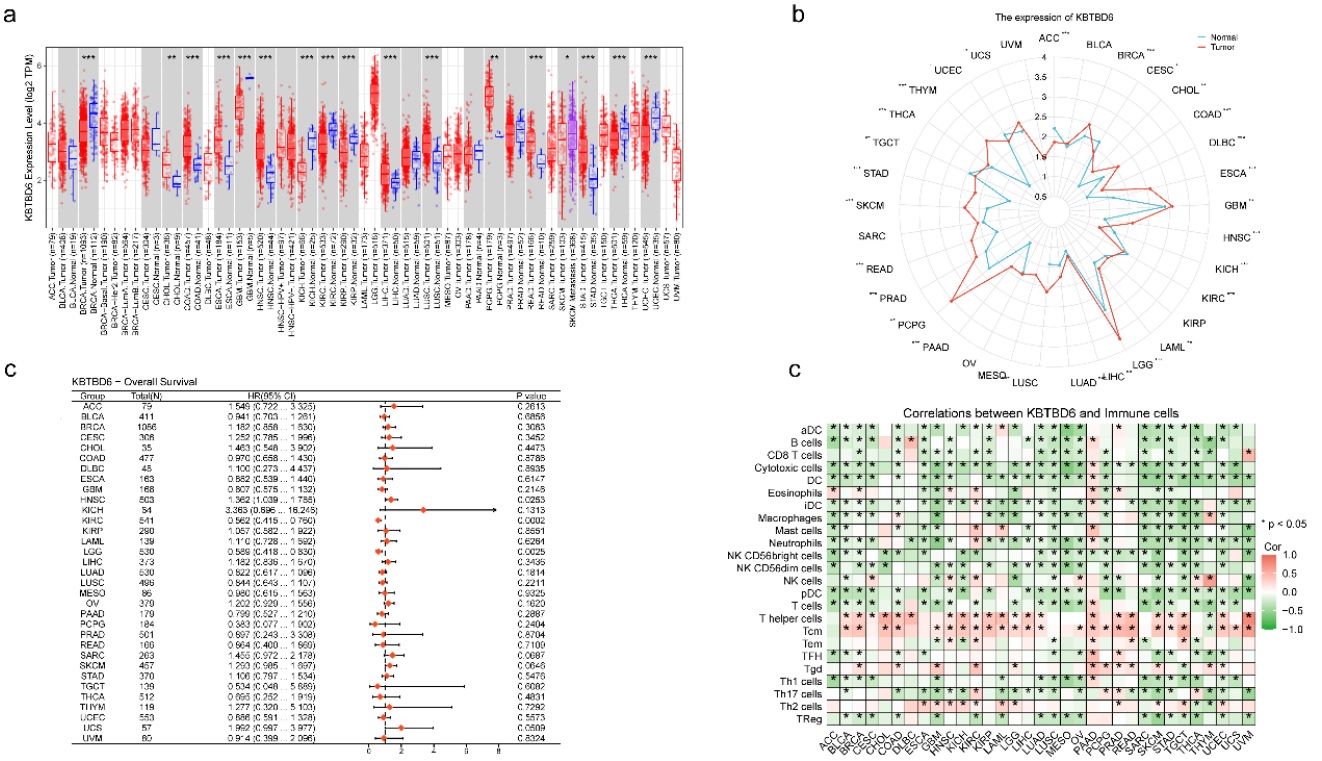

Figure 1. The performance of KBTBD6 in pan-cancer. **(a)** The expression of KBTBD6 in pan-cancer of the TCGA cohort. **(b)** The radar chart shows the expression of KBTBD6 in pan-cancer of the TCGA combined with GTEx cohort.*P < 0.05,**P < 0.01,***P < 0.001. **(c)** The prognostic forest plot shows the situation of KBTBD6 in the TCGA cohort. **(d)** The correlation between KBTBD6 and various immune cells in pan-cancer is shown in the form of a heatmap. *P < 0.05

3.2. KBTBD6 is closely related to prognosis and progression in OSCC

Analysis of the TCGA-OSCC cohort indicated that KBTBD6 expression was significantly elevated in OSCC tumor tissues, with further confirmation in paired tumor and normal tissue samples (**Figures 2a–b**). To evaluate the diagnostic potential of KBTBD6 in OSCC, ROC curve analysis was conducted. The area under the curve (AUC) was 0.870 (95% CI: 0.821–0.912), suggesting that KBTBD6 serves as a reliable diagnostic marker for OSCC (**Figure 2c**).

To further investigate the impact of KBTBD6 on prognosis in HNSC and OSCC, proportional hazards hypothesis testing and fitted survival regression analysis were conducted using the "survival" package. Results indicated that in both the HNSC and OSCC cohorts, patients in the KBTBD6^{high} group had worse overall survival (OS) compared to those in the KBTBD6^{low} group (**Figures 2d–e**). Additionally, analysis of OSCC clinical data revealed that KBTBD6 expression was lowest in G1 grade tumors, with a statistically significant increase from G1 to G2 and from G2 to G3 (**Figure 2f**). These findings indicate that KBTBD6 may serve as a prognostic and disease progression indicator in OSCC.

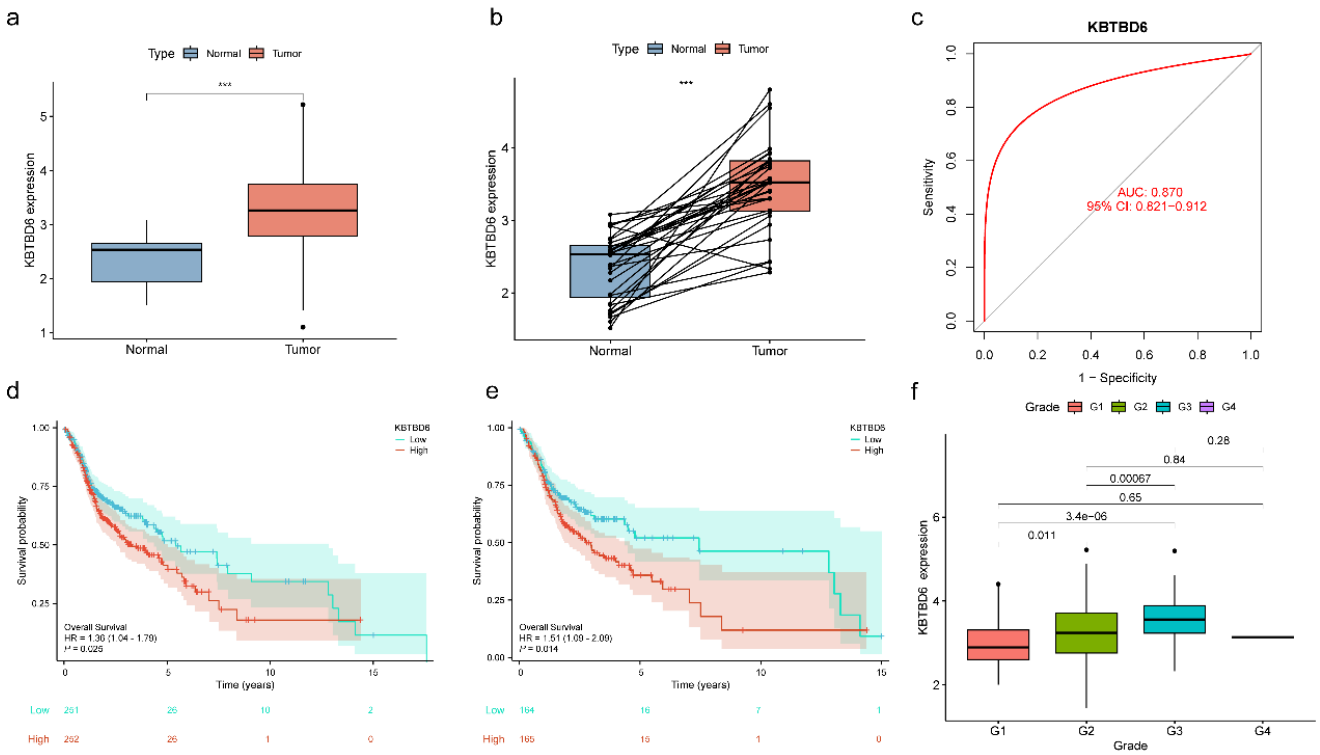

Figure 2. In OSCC, high expression of KBTBD6 is associated with a poor prognosis. **(a–b)** KBTBD6 expression in the OSCC (n = 346) and normal tissue (n = 32) samples in the TCGA cohort. ***P < 0.001, versus normal. **(c)** ROC curve of KBTBD6 for the diagnosis of OSCC. **(d)** Kaplan-Meier curves showing the overall survival (OS) of the KBTBD6^{high} and KBTBD6^{low} groups in HNSC. **(e)** Kaplan-Meier curves showing the overall survival (OS) of the KBTBD6^{high} and KBTBD6^{low} groups in OSCC. **(f)** Correlation between Grade of OSCC patients and KBTBD6 in the TCGA cohort

3.3. Construction of protein-protein interaction network

Genes correlated with KBTBD6 expression were identified from the TCGA-OSCC dataset, with the top four genes (*ADNP*, *KBTBD7*, *BRCA2*, and *NUFIP1*) shown to have strong correlations with *KBTBD6* (**Figures 3a–d**). To further investigate potential associations involving KBTBD6, 22 genes with a correlation coefficient above 0.6 were selected, and protein-protein interaction predictions were conducted. A network was then constructed to illustrate these connections (**Figure 3e**).

3.4. Potential functions of KBTBD6 in OSCC

The differential analysis identified 720 differentially expressed genes (DEGs) between the KBTBD6^{high} and KBTBD6^{low} groups, with the top 50 most significant DEGs displayed in a heatmap (**Figure 4a**). Gene Ontology (GO) analysis of these DEGs revealed associations with biological processes such as epidermal cell differentiation, keratinocyte differentiation, aminoacyltransferase activity, and epidermis development (**Figure 4b**). Consistent findings were observed in an enrichment function network analysis using the ClueGO plugin of Cytoscape (**Figure 4c**).

In addition, several cancer-related KEGG pathways, including cell adhesion molecules, growth hormone synthesis, secretion and action, AMP signaling pathway, ECM-receptor interaction, and IL-17 signaling pathway, showed significant enrichment among the DEGs (**Figures 4d–e**). These findings suggest that KBTBD6 may play a critical role in the progression of OSCC.

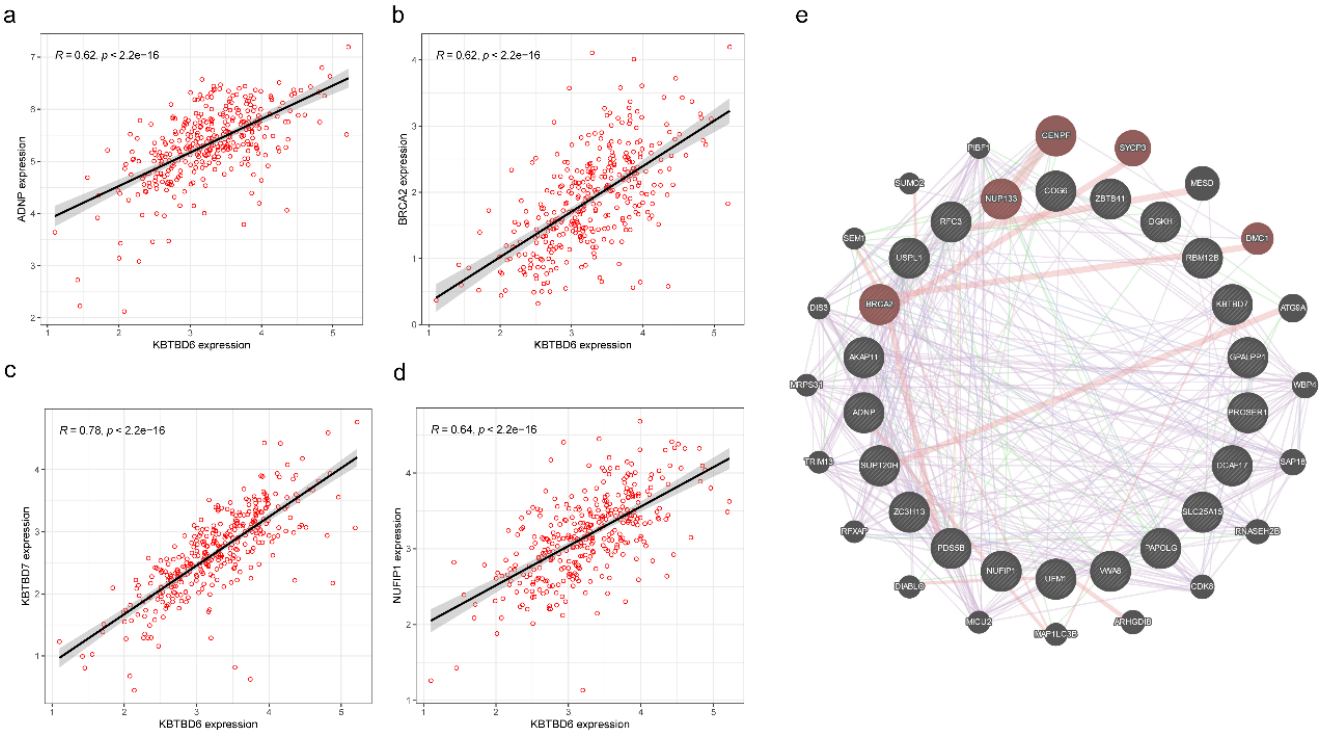

Figure 3. Genes co-expressed with *KBTBD6* in OSCC. **(a–d)** Top four genes co-expressed with *KBTBD6* in the TCGA-OSCC cohort. **(e)** PPI network of genes co-expressed with *KBTBD6*

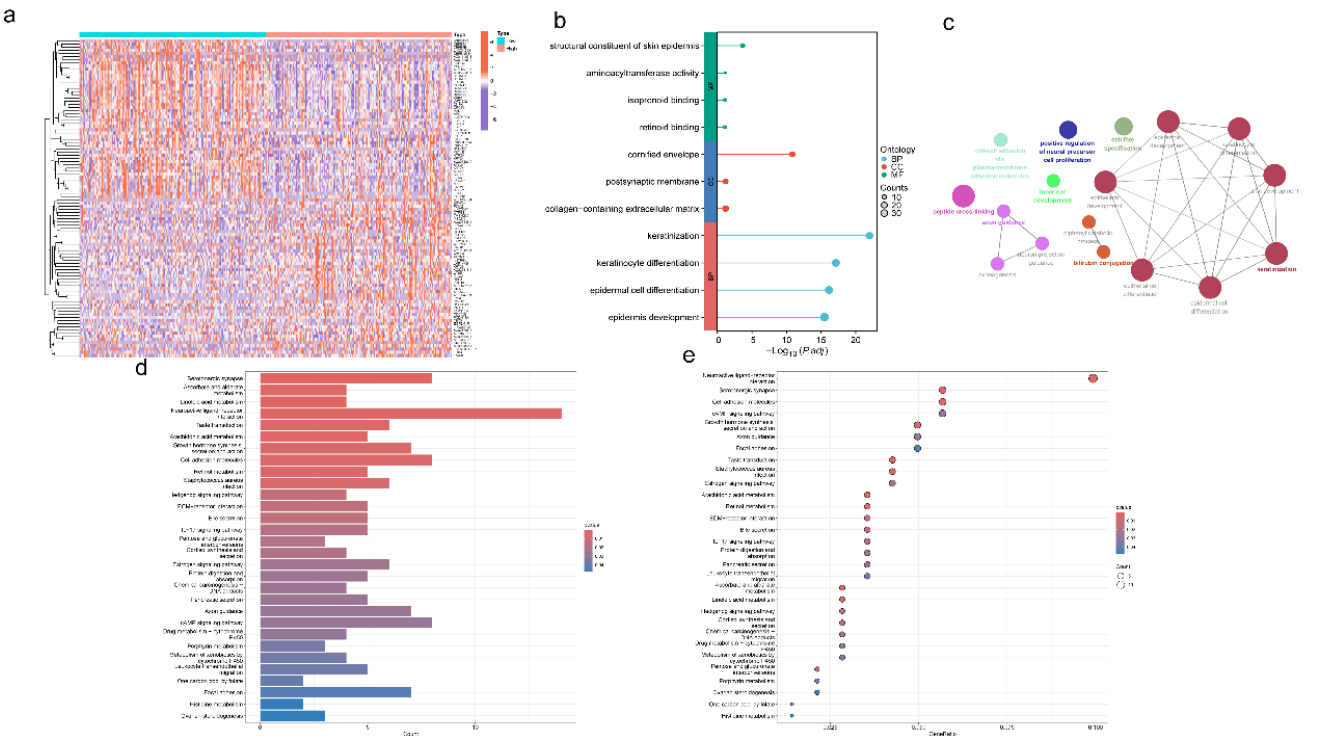

Figure 4. Functional role of KBTBD6 in OSCC. **(a)** Heatmap showing the DEGs between KBTBD6^{high} and KBTBD6^{low} groups. **(b–c)** Results of GO enrichment analysis. **(d–e)** Results of KEGG enrichment analysis

3.5. KBTBD6 and its association with the immune landscape in TSCC

The CIBERSORT algorithm was applied to assess the relationship between KBTBD6 and various immune cell subsets. Significant differences in T cells CD4 memory resting and neutrophils were observed between the KBTBD6^{high} and KBTBD6^{low} groups (**Figure 5a**). Immune infiltration scoring further analyzed the correlation between KBTBD6 and specific immune cells, showing that T cells CD4 memory resting, NK cells resting, and macrophages Mo are positively correlated with KBTBD6, while plasma cells, T cells CD8, T cells follicular helper, T cells gamma delta, monocytes, and neutrophils are negatively correlated (**Figures 5b–d**).

To explore KBTBD6's potential impact on immunotherapy, its association with immune checkpoints was analyzed. Results indicated that as KBTBD6 expression increases, there is a concurrent rise in the expression levels of immune checkpoint genes such as *TNFSF15*, *TNFSF4*, *CD80*, *CD70*, *CD86*, *CD40*, *NRP1*, *CD200R1*, *DE276*, *HAVCR2*, *TNFRSF9*, *CD160*, *CD44*, and *CD200* (**Figures 5e–f**). These findings suggest that KBTBD6 may play a role in modulating immune cells in OSCC.

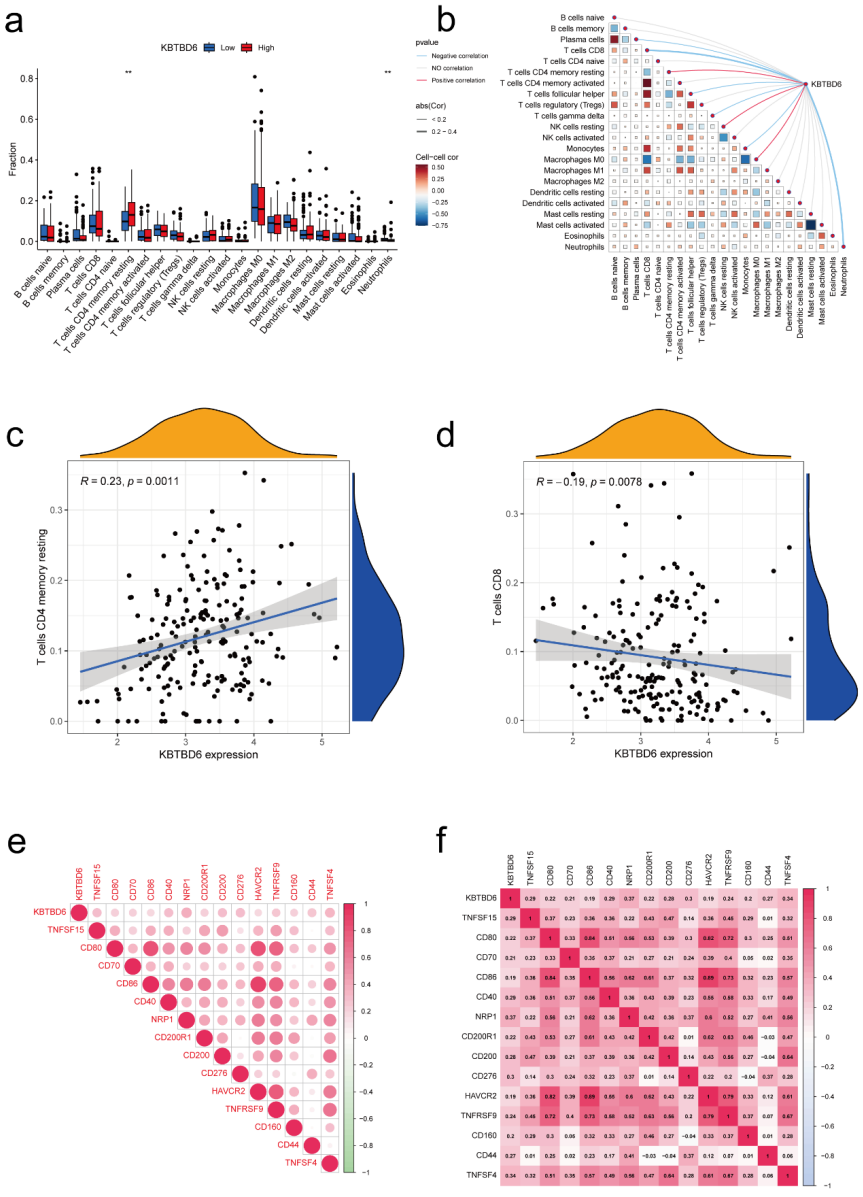

Figure 5. Correlation between KBTBD6 expression and immune infiltration in OSCC. **(a)** Differences in immune cell types between KBTBD6^{high} and KBTBD6^{low} groups. **(b–d)** Correlation between KBTBD6 expression and various immune cells. **(e–f)** Correlation between KBTBD6 expression and immune checkpoint genes.

3.6. Correlation between KBTBD6 expression and chemosensitivity

The sensitivity to several chemotherapeutic drugs in relation to KBTBD6 levels was evaluated using Cancer Genome Project (CGP) data. Low expression of KBTBD6 showed a significant correlation with increased sensitivity to AKT inhibitor VIII, bexarotene, bleomycin, thapsigargin, tipifarnib, and tubastatin A (**Figures 6a–f**). Thus, KBTBD6 expression levels may help predict OSCC patient responses to common chemotherapeutic agents, highlighting its potential as a biomarker for personalized treatment strategies.

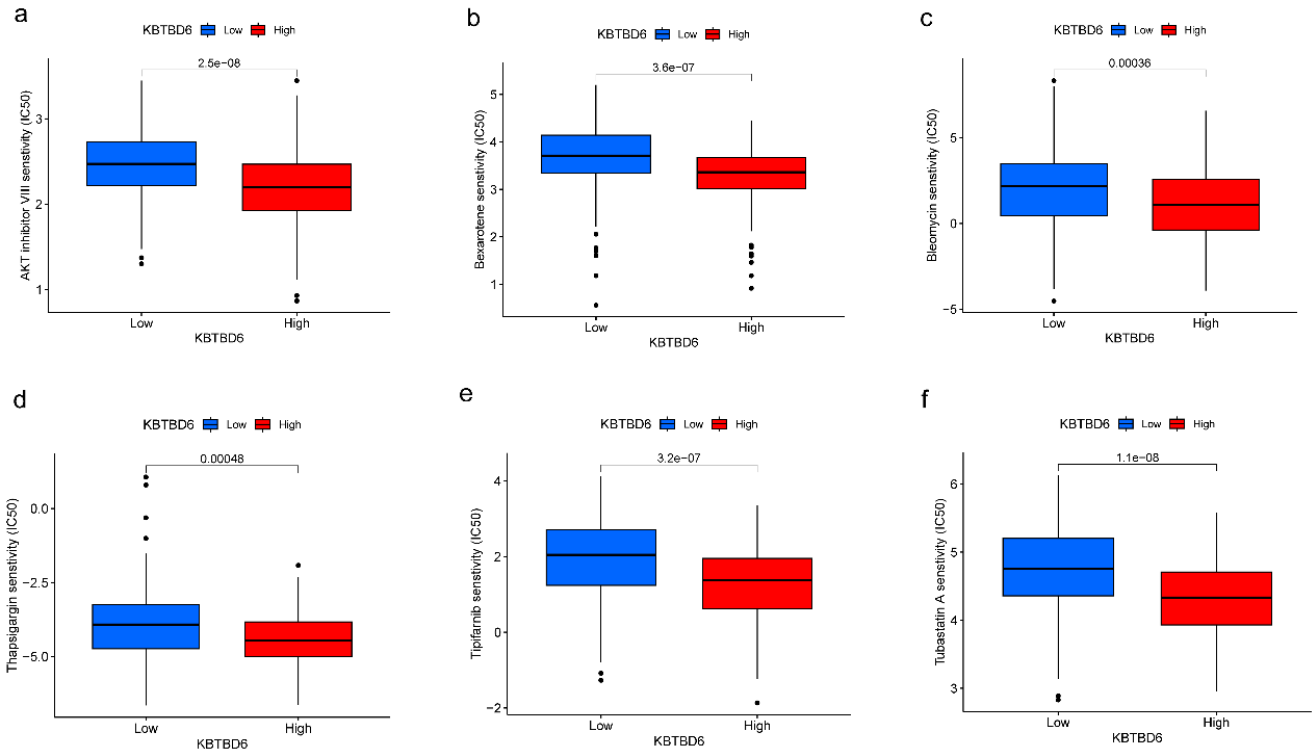

Figure 6. Correlation between KBTBD6 expression and chemosensitivity. IC_{50} values for **(a)** AKT inhibitor VIII, **(b)** bexarotene, **(c)** bleomycin, **(d)** thapsigargin, **(e)** tipifarnib, and **(f)** tubastatin A

3.7. Distribution of KBTBD6 in tumor subpopulations

The distribution pattern of KBTBD6 was analyzed using the single-cell transcriptome data from GSE172577. A total of 35 cell clusters were identified and classified into 11 different cell types, including endothelial cells, $CD8^+$ T cells, keratinocytes, ductal cells, NK cells, epithelial cells, gland cells, malignant cells, mast cells, regulatory T cells (Treg cells), and monocytes/macrophages, based on marker gene expression (**Figures 7a–b**). KBTBD6 expression was relatively low in endothelial and epithelial cells, while it was higher in $CD8^+$ T cells, ductal cells, gland cells, keratinocytes, malignant cells, mast cells, monocytes/macrophages, and NK cells. Although KBTBD6 expression was high in Treg cells, significant variability was observed among samples, indicating inter-patient differences (**Figures 7c–d**).

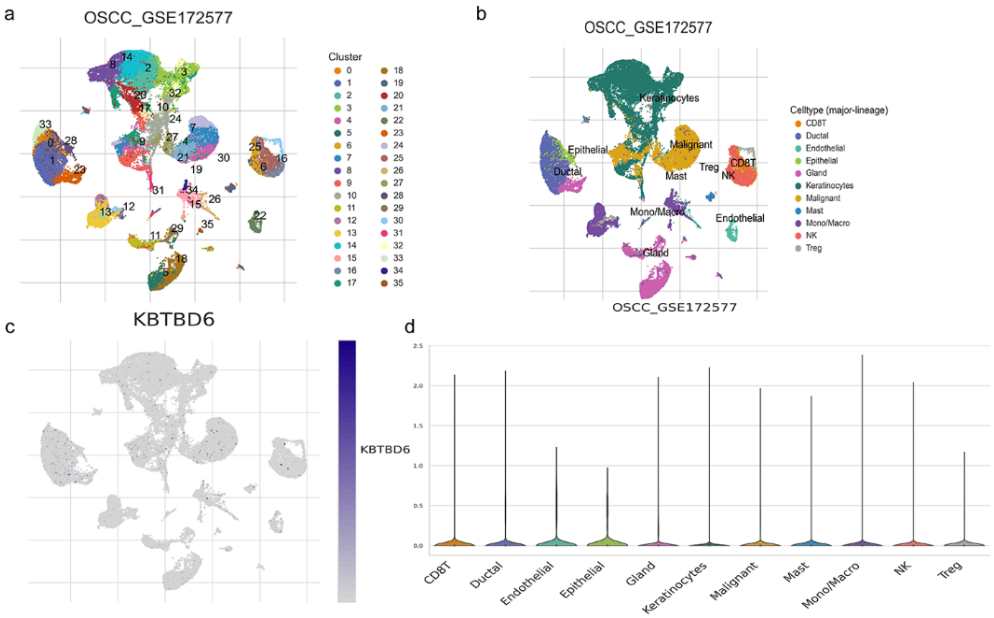

Figure 7. KBTBD6 expression in different cell populations in OSCC. **(a)** UMAP clustering of the OSCC_GSE17257 dataset. **(b)** UMAP clustering of the 11 cell types in the OSCC_GSE17257 dataset. **(c–d)** KBTBD6 expression pattern across cell types.

3.8. Knockdown of KBTBD6 inhibits OSCC growth

KBTBD6 protein expression in tissue microarrays of OSCC and normal tissues was evaluated, revealing higher levels in tumor tissues, consistent with TCGA analysis (**Figures 8a–b**). KBTBD6 expression was knocked down, resulting in a significant reduction of KBTBD6 mRNA levels in SCC9 and SCC25 cells with siKBTBD6 treatment (**Figure 8c**). KBTBD6 silencing also decreased cell viability in SCC9 and SCC25 cells, as determined by CCK-8 assays (**Figures 8d–e**). Overall, KBTBD6 silencing was found to suppress OSCC growth.

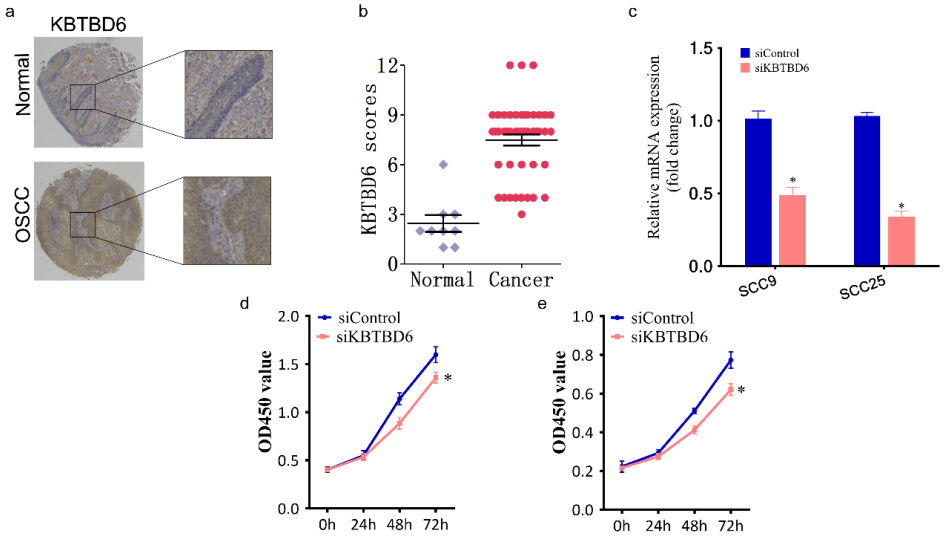

Figure 8. KBTBD6 regulates OSCC cell growth. **(a–b)** Representative images and scores of KBTBD6 expression in OSCC (n = 45) and normal tissues (n = 9). **(c)** Relative KBTBD6 mRNA expression in SCC9 and SCC25 cells transfected with siControl and siKBTBD6. **(d)** Cell viability of SCC9 cells transfected with siControl and siKBTBD6. **(e)** Cell viability of SCC25 cells transfected with siControl and siKBTBD6. Data represent the mean ± SEM of at least three independent experiments. *$P < 0.05$, vs. siControl

4. Discussion

OSCC is a common malignant tumor of the head and neck, with a complex pathogenesis involving multiple risk factors, including long-term smoking, alcohol consumption, poor oral hygiene, viral infections, environmental influences, and genetics [2]. Despite advancements in treatment, while early detection and treatment have improved patient survival rates, advanced OSCC still shows a high propensity for recurrence and metastasis, often resulting in poor prognosis [17]. Thus, it remains essential to deepen the understanding of OSCC pathogenesis and to identify more effective diagnostic and therapeutic strategies.

KBTBD6 is an important protein-coding gene involved in protein interactions and ubiquitination. *KBTBD7*, a related gene, plays a key role in cancer development and is a known prognostic marker in NSCLC [18]. However, the specific role of KBTBD6 in tumors remains unclear. This study conducted an in-depth investigation into KBTBD6 expression patterns across various tumors, its prognostic significance, and its correlation with immune cells using data from the TCGA pan-cancer cohort. Pan-cancer analysis revealed aberrant expression of KBTBD6 in cancers such as BRCA, COAD, HNSC, KICH, and UCEC. In addition, a joint analysis of TCGA and GTEx databases showed that KBTBD6 expression was elevated in BRCA, COAD, DLBC, ESCA, HNSC, and LGG tissues compared to normal tissues [19]. To assess the impact of this aberrant expression on patient prognosis, pan-cancer survival analysis of the TCGA cohort revealed statistically significant associations in HNSC, KIRC, and LGG, with an HR of 1.362 in HNSC, indicating KBTBD6 may be a risk factor in this cancer type. Correlation analysis using the ssGSEA algorithm further demonstrated that KBTBD6 is closely linked to various immune cells, predominantly with a negative correlation [20].

Further analysis of OSCC, a major subtype of HNSC, using the TCGA database showed that KBTBD6 expression in OSCC tissues was significantly elevated compared to normal tissues [21]. The AUC for KBTBD6 in OSCC was 0.870, suggesting its reliability as a diagnostic marker [22]. Survival analysis based on clinical data indicated that elevated KBTBD6 expression is associated with a poorer prognosis in HNSC and OSCC patients. Additionally, the expression of KBTBD6 correlated with tumor grade, with higher levels associated with more advanced grades, linking elevated KBTBD6 expression with poorer prognosis and disease progression. Co-expression analysis identified 22 genes with a high correlation to *KBTBD6* in OSCC, and a protein-protein interaction network was constructed using the GeneMANIA database [14]. Among these genes, *ADNP*, *BRCA2*, *KBTBD7*, and *NUFIP1* have strong associations with tumors. For instance, *ADNP* promotes cell proliferation in bladder cancer [23], *BRCA2* is a susceptibility gene in breast cancer [24], and cancer-associated fibroblasts mediate *NUFIP1* to support pancreatic cancer progression [25]. The KEGG results suggest that KBTBD6 may participate in several pathways, including the IL-17 signaling pathway, cAMP signaling pathway, ECM-receptor interaction, chemical carcinogenesis, and cell adhesion molecules pathways [26,27]. Extracellular vesicles in OSCC may influence the microenvironment, leading to cytokine imbalance and activation of the IL-17 signaling pathway, promoting tumor progression [28,29]. Furthermore, cell adhesion molecules (CAMs) contribute to tumor proliferation and metastasis by regulating cell adhesion within the tumor microenvironment [27,30], indicating that KBTBD6 may influence tumor progression through various pathways.

The immune microenvironment plays a crucial role in tumor development. Analysis indicated a significant association between KBTBD6 and the immune landscape of OSCC, with positive correlations with T cells CD4 memory resting, and CD8 T cells [31,32]. Immune checkpoint analysis further revealed that increased KBTBD6 expression is positively correlated with several immune checkpoints, potentially enabling immune evasion by inhibiting immune cell attacks on tumors [33]. This finding aligns with KBTBD6's association with tumor

severity and the critical role of T cells in immunotherapy. Analysis of the GEO single-cell dataset showed elevated KBTBD6 expression in $CD8^+$ T cells, suggesting its potential to modulate immune cell functions within tumors. Specifically, KBTBD6 may regulate the cytotoxic activity of $CD8^+$ T cells, potentially weakening their capacity to eliminate tumor cells and promoting immune escape [34]. Additionally, elevated KBTBD6 expression in ductal and glandular cells may contribute to malignant transformations in these cell types [35]. Certain cases exhibit lower KBTBD6 expression in regulatory T cells, possibly compromising immunosuppressive functions and facilitating tumor progression [36].

While surgery is the preferred treatment for early-stage OSCC, chemotherapy remains essential for intermediate and advanced stages. Analysis indicated that OSCC patients with low KBTBD6 expression may respond favorably to drugs such as AKT inhibitor VIII, bexarotene, bleomycin, thapsigargin, tipifarnib, and tubastatin A, suggesting that KBTBD6 expression could serve as a predictor of drug sensitivity, aiding in the development of individualized treatments to reduce drug resistance. Tissue microarray analysis confirmed higher KBTBD6 expression in OSCC tissues compared to normal tissues. In vitro studies using siRNA technology to downregulate KBTBD6 expression significantly inhibited OSCC cell growth, supporting bioinformatics predictions that link KBTBD6 to poor prognosis in OSCC. Nonetheless, additional studies are necessary to validate these findings, and further exploration is needed to clarify the specific mechanisms and functions of KBTBD6 in OSCC progression.

5. Conclusion

KBTBD6 is overexpressed in OSCC patients and correlates with prognosis, clinical stage, and immune infiltration. These findings suggest that KBTBD6 may offer a novel perspective for the prediction, diagnosis, and treatment of OSCC.

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Availability of data and materials

The data that support the findings of this study are openly available in The Cancer Genome Atlas at https://portal.gdc.cancer.gov/.

Disclosure statement

The authors declare no conflict of interest.

Author contributions

Conceptualization: Dunhui Yang, Xijia Wang
Methodology: Dunhui Yang
Software: Kang Li

Formal analysis: Dunhui Yang, Xiaorui Geng
Investigation: Huifei Lu, Kang Li, Xiaorui Geng
Writing – original draft: Dunhui Yang, Xiaorui Geng
Writing – review & editing: all authors

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