

# CLEC10A is A Prognostic Biomarker and is Correlated with Immune Infiltrates in Breast Cancer

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## Primary research

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# Abstract

## Background

To investigate the association between CLEC10A and prognosis in breast cancer (BC) patients.

## Methods

We assessed the prognostic value of CLEC10A in BC using data from The Cancer Genome Atlas (TCGA) online database. We examined CLEC10A expression differences in BC and normal tissues via the TIMER and UALCAN databases. Then, we used the Kaplan-Meier plotter database to evaluate the correlation of CLEC10A mRNA levels with clinical outcomes. Subsequently, the TIMER platform and TISIDB website were used to assess the correlation of CLEC10A with the tumor immune cell infiltration level in BC.

## Results

Our results showed that CLEC10A levels were significantly downregulated in BC tissues compared with normal tissues. CLEC10A expression was associated with histologic type, pathologic stage, T stage, Her2 status and a poor prognosis. Additionally, CLEC10A was positively related to the level of different tumor-infiltrating immune cells in BC, and CLEC10A was closely correlated with the gene markers of diverse immune cells. Additionally, low CLEC10A expression predicted a poor prognosis in BC patients grouped based on immune cell infiltration levels.

## Conclusion

CLEC10A may be a potential biomarker and may efficiently predict prognosis in BC patients.

## Introduction

Breast cancer (BC), the most common female cancer, is reported to be the second-leading cause of cancer-related death, and a considerable threat to female health globally [1]. BC can be subdivided into four molecular subtypes: luminal A (estrogen receptor [ER] + or progesterone receptor [PR] + and human epidermal growth factor receptor-2 [HER2]-), luminal B (ER + and/or PR + and HER2+), basal-like subtypes (ER-, PR-, HER2-, cytokeratin [CK]5/6+, and epidermal growth factor receptor [EGFR]+), and HER2 overexpressing (ER-, PR-, and HER2+) [2]. The initial treatment methods for BC are surgery, chemotherapy, endocrine therapy and radiation therapy, which greatly improve the outcomes [3, 4]. Classical clinical prognostic biomarkers, such as ER, PR, and HER2 continue to play a significant role in the identification of patients who may benefit from endocrine therapy or targeted therapy [4]. Although the management of breast cancer, including early diagnosis and effective therapeutic measures, has progressed rapidly over the past few decades, metastasis is still the major cause of a poor prognosis in BC patients [5]. Based on

tumor heterogeneity, the available biomarkers that can predict BC prognosis still have some limitations. thus, the demand for novel effective biomarkers as prognostic indicators and individualized treatments is highly desirable and urgent.

C-type lectin domain family 10, member A (CLEC10A), a member of the CLR family, is also named macrophage galactose type C-type lectin (MGL) [6]. CLEC10A, like other members of the CLR family, has been shown to be involved in improving the immune activity of immune cells [6]. CLEC10A recognizes and acts on Tn antigens associated with tumors, and is one of the effective antigen presentation proteins of CD4 T cells that facilitates immune responses. Furthermore, CLEC10A binding with tumor associated antigens carrying  $\alpha$ -N-acetylgalactosamine can significantly improve antigen-specific CD8 T cell activation [6, 7]. Tumor-specific CD8 and CD4 T cells are required for effective tumor eradication. The function of CLEC10A in promoting the antitumor activity of immune cells has clearly attracted increasing attention and has been proposed as a target for cancer immunotherapy [7]. It was reported that low expression of CLEC10A in lung cancer was associated with a poor clinical prognosis [8]. However, its clinical significance and biological function in BC remain unclear.

In our study, we conducted a comprehensive analysis of the correlation between CLEC10A expression and the risk of BC progression based on the TCGA database, and then assessed the correlation of different CLEC10A expression levels with alterations in the tumor immune microenvironment. The results revealed the significant prognostic value of CLEC10A expression and indicated it as a potentially promising target for immunotherapeutic strategies in BC.

## Materials And Methods

### Xiantao Database Analysis

The Xiantao database (<https://www.xiantao.love/products>) integrates literature and databases of tumor microarray results and is mainly used for gene expression analysis, coexpression analysis, enrichment analysis and interaction network analysis. We used the Xiantao database to analyze CLEC10A expression in various cancer types.

### Timer Database Analysis

The Tumor Immune Estimation Resource (TIMER) database (<https://cistrome.shinyapps.io/timer/>) is a comprehensive resource for the analysis of gene expression and tumor-infiltrating immune cells across different cancer types. This web assesses the abundances of six types of tumor-infiltrating cells (B cells, CD4 + T cells, CD8 + T cells, neutrophils, macrophages, and dendritic cells), using the TIMER algorithm [9]. We used the TIMER website to analyze the differential expression of CLEC10A in tumor and normal tissues in BC patients. Moreover, we evaluated the correlation of CLEC10A with the infiltration of tumor immune cell types and the molecular marker expression of different immune cell types.

# Ualcan Database Analysis

The UALCAN database (<http://ualcan.path.uab.edu/index.html>) is available for online analysis of differential gene expression in cancer and normal tissue from The Cancer Genome Atlas (TCGA) RNA sequencing datasets and clinical datasets [10]. In addition, this website provides survival prognosis data based on gene expression differences in 31 cancer types. This study used the UALCAN database to validate the analysis results of the Xiantao database, and further determined the correlations between CLEC10A gene expression and clinical features. Differences with  $p < 0.05$  were considered statistically significant.

# Kaplan-meier Plotter Database Analysis

Kaplan-Meier plotter (<http://kmplot.com/analysis/>) is an open, intuitive portal tool for prognostic analysis, that was used to assess the relationship between clinical outcomes and CLEC10A expression in different cancers [11]. We performed a prognostic analysis based on CLEC10A expression levels in relevant immune cell subgroups using this website. We calculated the hazard ratios (HRs), 95% confidence intervals (CIs) and log-rank p-values.

# TISIDB

The TISIDB database (<http://cis.Hku.hk/TISIDB/>) is a portal for analyzing tumor and immune cell interactions that integrates multiple heterogeneous data types [12]. For this study, TISIDB provided the correlations between CLEC10A expression and tumor-infiltrating lymphocytes.

# Statistical Analysis

CLEC10A expression was analyzed via the Xiantao, TIMER, UALCAN and TISIDB databases. Survival curves were generated using the Kaplan-Meier plotter database and R project using the “survival” package. We used Spearman’s correlation analysis to evaluate the correlation of gene expression in the TIMER. Differences with  $p < 0.05$  were considered statistically significant.

# Results

## The CLEC10A mRNA expression in different cancers

We analyzed the mRNA expression of CLEC10A using the Xiantao database and TIMER website. The results showed that CLEC10A was significantly lower in most cancer tissues, than in corresponding normal tissues (Fig. 1A). In addition, we used the UALCAN database to validate the findings in the TIMER website and reported lower expression of CLEC10A in paired and nonpaired BC tissues than in normal tissues (Fig. 1B, C). In addition, CLEC10A expression was associated with pathologic stage, histological

type, T stage and HER2 status (Fig. 1D-F, K), but not with N stage, M stage, ER status or PR status (Fig. 1G-J).

## Prognostic Significance Of Clec10a Expression In Bc

We investigated the Kaplan-Meier plotter database for the prognostic significance of

CLEC10A expression in BC. Low levels of CLEC10A predicted poor prognosis in BC (Fig. 2A, C). As Kaplan-Meier plotter analyses only OS, disease-specific survival (DSS) and progression-free intervals (PFI) values, we assessed the multiple clinical prognostic value of CLEC10A in a variety of cancers by R project using the “survival” package. Forest plot showed CLEC10A as a risk factor for different prognoses in BC (Fig. 3A, C). These findings indicated that CLEC10A is a preventative factor in BC.

## Clec10a Expression Is Correlated With Immune Infiltration In Bc

Tumor-infiltrating lymphocytes can independently predict sentinel lymphnode status and prognosis in various cancers [8]. Therefore, we used TIMER to analyze the correlation of CLEC10A levels with immune infiltration levels in BC. The results showed that CLEC10A expression was significantly positively correlated with the infiltration of B cells ( $r = 0.257$ ,  $p = 3.65e-16$ ), CD4 + T cells ( $r = 0.577$ ,  $p = 1.21e-86$ ), CD8 + T cells ( $r = 0.439$ ,  $p = 3.42e-47$ ), macrophages ( $r = 0.117$ ,  $p = 2.30e-04$ ), dendritic cells ( $r = 0.531$ ,  $p = 2.04e-70$ ) and neutrophils ( $r = 0.402$ ,  $p = 2.94e-38$ ) in BC (Fig. 4A). Then, we used the TISIDB database to further explore the relationship between CLEC10A levels and 28 tumor immune infiltrating cell subtypes. These results showed that CLEC10A was associated with all immune cell subtypes in BC (Fig. 4B, Table 1). In particular, activated CD8 T cells (Act\_CD8) ( $r = 0.592$ ,  $p < 2.2e-16$ ), central memory CD8 + T cells (Tcm\_CD8) ( $r = 0.134$ ,  $p < 8.571e-6$ ), activated CD4 T cells (Act\_CD4) ( $r = 0.385$ ,  $p < 2.2e-16$ ), central memory CD4 + T cells (Tcm\_CD4) ( $r = 0.296$ ,  $p < 7.3e-24$ ), type 2 T helper cells ( $r = 0.315$ ,  $p < 2.2e-16$ ), type 1 T helper cells ( $r = 0.69$ ,  $p < 2.2e-16$ ) and CLEC10A were moderately correlated with CLEC10A expression (Fig. 4C-H). Notably, macrophages ( $r = 0.585$ ,  $p < 2.2e-16$ ) also displayed a moderate correlation with CLEC10A expression (Fig. 4I). These results strongly implicate CLEC10A as a major tumor immune infiltration regulator in BC.

## Clec10a Expression Is Associated With Immune Cell Type Markers

We assessed the correlation between CLEC10A expression and tumor-infiltrating immune cell gene marker levels in BC tissues by exploring the TIMER database. Our results showed that the CLEC10A level in BC tissues was strongly associated with immune markers of B cells, CD8 T cells, M2 macrophages, monocytes, natural killer (NK) cells, T cells (general), dendritic cells (DCs), T helper cells, Tregs, and T

exhaustion cells (Table 1). Notably, we found that the CLEC10A level was significantly correlated with the levels of various subtypes of T cell markers, including CD8 + T markers, CD8A and CD8B; T cell (general) markers, CD3D, CD3E, and CD2; exhausted T cell markers CTLA4, HAVCR2, GZMB, LAG-3, and PD-1; Th2 markers; Th17 markers STAT6, STAT5A, and IL17A; Treg markers FOXP3, CCR8, STAT5B, and TGFB1; Tfh marker BCL6; and neutrophil markers ITGAM and CCR7, etc (Table 2). Significant correlations of CLEC10A levels with different macrophage markers (M2 macrophage markers MS4A4A, VSIG4 and CD163; monocyte markers CSF1R and CD86; tumor-associated macrophage (TAM) markers CD68, IL21, IL10, and CCL2; and B cell markers CD19 and CD79A) (Table 2). Furthermore, the expression of CLEC10A was not markedly related to marker genes for DC markers, CD1C, NOS2, CEACAM8, Th2, GATA3, Th17 cells and STATA3 in BC. These findings reveal that CLEC10A is involved in the regulation of tumor immune infiltration in BC.

Table 1 The correlation between CLEC10A expression and tumor lymphocyte infiltration in human cancer (TISIDB).

	<b>r</b>	<b>p</b>
Activated CD8 T cell (Act_CD8)	0.59	2.2e-16
Central memory CD8 T cell (Tcm_CD8)	0.134	8.57E-06
Effector memory CD8 T cell (Tem_CD8)	0.701	<2.2e-16
Activated CD4 T cell (Act_CD4)	0.382	<2.2e-16
Central memory CD4T cell (Tcm_CD4)	0.296	7.30E-24
Effector memory CD4 T cell (Tem_CD4)	0.392	<2.2e-16
T follicular helper cell(Tfh)	0.607	<2.2e-16
Gamma delta T cell (Tgd)	0.434	<2.2e-16
Type 1 T helper cell (Th1)	0.69	<2.2e-16
Type 17 T helper cell (Th17)	0.526	<2.2e-16
Type 2 T helper cell (Th2)	0.315	<2.2e-16
Regulatory T cell (Treg)	0.504	<2.2e-16
Activated B cell (Act_B)	0.782	<2.2e-16
Immature B cell (Imm_B)	0.688	<2.2e-16
Memory B cell (Mem_B)	0.381	<2.2e-16
natural killer cell (NK)	0.464	<2.2e-16
CD56bright natural killer cell (CD56bright)	0.388	<2.2e-16
CD56dim natural killer cell (CD56dim)	0.209	3.02E-10
Myeloid derived suppressor cell (MDSC)	0.566	<2.2e-16
Natural killer T cell (NKT)	0.576	<2.2e-16
Activated dendritic cell (Act_DC)	0.326	<2.2e-16
Plasmacytoid dendritic cell (pDC)	0.353	<2.2e-16
Immature dendritic cell (iDC)	0.098	0.00111
Macrophage (Macrophage)	0.585	<2.2e-16

	<b>r</b>	<b>p</b>
Eosinophi (Eosinophil)	0.601	<2.2e-16
Mast (Mast)	0.685	<2.2e-16
Monocyte (Monocyte)	0.483	<2.2e-16
Neutrophil (Neutrophil)	0.359	<2.2e-16

Table2 Correlation analysis between CLEC10A and relate genes and markers of immune cells in TIMER

Description	Gene markers	None		Purity	
		COR	P	COR	P
B CELL	CD19	0.655	***	0.532	***
	CD79A	0.65	***	0.511	***
CD8 T CELL	CD8A	0.726	***	0.507	***
	CD8B	0.677	***	0.565	***
DENDRITIC CELL	ITGAX	0.492	***	0.343	***
	NRP1	0.273	***	0.121	***
	CD1C	0.876	0.923	0.819	***
	HLA-DPA1	0.642	***	0.511	***
	HLA-DRA	0.648	***	0.514	***
	HLA-DQB1	0.535	***	0.411	***
	HLA-DPB1	0.715	***	0.586	***
	PTGS2	0.415	***	0.284	***
M1 MACROPHAGE	IRF5	0.307	***	0.226	***
	NOS2	0.011	0.72	0.022	0.493
	MS4A4A	0.554	***	0.43	***
M2 MACROPHAGE	VSIG4	0.399	***	0.272	***
	CD163	0.44	***	0.327	***
	CSF1R	0.549	***	0.444	***
MONOCYTE	CD86	0.475	***	0.338	***
	KIR2DS4	0.332	***	0.234	***
NATURAL KILLER CELL	KIR3DL3	0.235	***	0.181	***
	KIR3DL2	0.469	***	0.356	***
	KIR3DL1	0.432	***	0.34	***
	KIR2DL4	0.388	***	0.279	***
	KIR2DL3	0.356	***	0.266	***
	KIR2DL1	0.34	***	0.255	***

\*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001.

Description	Gene markers	None		Purity	
NEUTROPHILS	CCR7	0.792	***	0.52	***
	ITGAM	0.392	***	0.338	***
	CEACAM8	0.041	0.178	0.005	0.886
T CELL GENERAL	CD3D	0.771	***	0.549	***
	CD3E	0.782	***	0.56	***
	CD2	0.735	***	0.528	***
T CELL EXHAUSTION	CTLA4	0.57	***	0.44	***
	LAG3	0.387	***	0.286	***
	HAVCR2	0.393	***	0.252	***
	GZMB	0.625	***	0.508	***
	PDCD1	0.675	***	0.552	***
TAM	CCL2	0.472	***	0.338	***
	IL10	0.455	***	0.334	***
	CD68	0.42	***	0.288	***
	BCL6	0.126	***	0.083	**
	IL21	0.367	***	0.279	***
TH1	TBX21	0.745	***	0.643	***
	STAT4	0.686	***	0.554	***
	STAT1	0.255	***	0.184	***
	IFNG	0.52	***	0.404	***
	IL13	0.273	***	0.216	***
TH2	GATA3	-0.198	***	-0.061	0.056
	STAT6	0.249	***	0.223	***
	STAT5A	0.424	***	0.31	***
TH17	STAT3	0.083	***	0.038	0.229
	IL17A	0.203	***	0.102	***
TREG	FOXP3	0.525	***	0.384	***
*p < 0.05, **p < 0.01, ***p < 0.001.					

Description	Gene markers	None		Purity	
	CCR8	0.42	***	0.333	***
	STAT5B	0.234	***	0.207	***
	TGFB1	0.411	***	0.263	***
*p < 0.05, **p < 0.01, ***p < 0.001.					

### Prognostic potential of CLEC10A in different tumors based on immune cells

This study showed that the CLEC10A level was associated with the immune infiltration of BC. Additionally, downregulated CLEC10A has a poor prognosis in BC patients. Thus, we propose a hypothesis that CLEC10A may affect the prognosis of BC patients partly through immune infiltration. We performed Kaplan-Meier plotter analyses of CLEC10A expression in BC and considered the infiltration level of B cells, CD4 + memory T cells, CD8 + T cells, macrophages, neutrophils, NK T cells, mesenchymal stem cells, regulatory T cells, Th1 cells, and Th2 cells. We found that BC samples with high CLEC10A levels were enriched in CD4 + memory T cells (p = 0.04), neutrophils (p = 0.032), macrophages (p = 0.002), natural killer T cells (p = 0.017), Treg cells (p = 0.04), and Th2 cells (p = 0.0018) (Fig. 5B, D, E, G, H, J). Unfortunately, there was no significant difference between the high and low CLEC10A expression groups in terms of OS for patients with high infiltration of B cells (p = 0.15), CD8 + T cells (p = 0.34), mesenchymal stem cells (p = 0.06), and Th1 cells (p = 0.1) (Fig. 5A, C, F, I). The above analysis suggested that immune infiltration may affect the prognosis of BC patients with low CLEC10A expression.

## Discussion

Breast cancer has an intrinsically complex tumor microenvironment (TME), which plays a central role in the pathogenesis of BC [13]. The TME can be divided into two parts: tumor cells and the surrounding extracellular matrix (ECM) [14]. The ECM is a complex network composed of collagenous and noncollagenous components, which are critical determinants of interstitial transport [15]. ECM proteins mainly comprise collagen I, collagen IV, fibronectin and laminin, which provide biochemical reagents and structural support for the growth of tumor cell [15]. Furthermore, immune cells of the TME influence the course of tumor progression and become the key to overall efficacy [16].

CLEC10A has been reported to be associated with improving the immune response of immune cells. Recently, more attention has been given to CLEC10A's ability to influence the antitumor immune response and proposed that it may serve as a therapeutic target in most tumor therapies [6, 7]. In our study, we first investigated the relationships of CLEC10A with immune cell infiltrates in relation to tumor cells as well as its expression and prognostic significance.

In this study, we found that CLEC10A expression was decreased in BC tissues compared to normal tissues. We also found that CLEC10A expression was associated with tumor pathological stage, histological type, T stage, and HER2 status in BC. Moreover, the low CLEC10A level was related to stage

IV disease and the infiltrating ductal carcinoma subtype (Fig. 1). These results indicate that low expression of CLEC10A may play a crucial role in tumor progression. Our findings are consistent with those of a previous study [8]. CLEC10A expression was decreased in some cancer tissues and associated with clinicopathological features, including T stage and N stage.

Our results showed that low CLEC10A expression was correlated with poor OS, DSS, and PFI (Fig. 2A, C) in BC, which was in agreement with previous findings that low expression of CLEC10A was associated with tumor growth and a poor prognosis in lung carcinoma [8]. Eggink et al [7] reported that CLEC10A could promote the infiltration of immune cells into the tumor to inhibit tumor growth and metastasis. Our results imply that CLEC10A could be used as a powerful prognostic biomarker with potential therapeutic benefit in BC clinical management.

CLEC10A recognizes and acts on tumor-associated Tn antigens and can efficiently present antigens to CD4 T cells [7]. CLEC10A could significantly increase the activation of antigen-specific CD8 T cells by binding with tumor-associated antigens carrying  $\alpha$ -N-acetylgalactosamine. In the present study, we demonstrated that CLEC10A expression is related to some immune infiltrating cells in BC (Fig. 4). Efficient CLEC10A binding requires multivalent ligands and a corresponding multivalent binder, such as a fragment of the MUC1 protein provide orders of magnitude greater avidity to the receptor. The structure of the ligand influences the cellular response, with large Tn-bearing glycoproteins trapped in an endolysosomal compartment, whereas smaller glycopeptides are further processed HLA I/HLA II compartments [17]. CLEC10A binds to the related ligand and induces the maturation of immune cells to combat tumor progression [18, 19].

Additionally, we analyzed markers of the immune system in BC. After cell purity correction, CLEC10A was positively correlated with many immune cell markers in BC (Table 2). The results further imply that CLEC10A is associated with immune infiltration in BC. Notably, increased CLEC10A levels were positively associated with Treg and T cell exhaustion markers. There was a significant correlation between CLEC10A levels and several T helper cell (Th1, Th2) markers in BC. These connections may indicate the underlying mechanisms by which CLEC10A regulates T cell function in BC. Therefore, CLEC10A may confer a poor prognosis in BC patients by recruiting and regulating immune cells.

The results of the KaplanMeier plotter database analysis showed that samples with high expression levels of CLEC10A were enriched in a variety of immune cell cohorts, and this phenotype was related to a poor prognosis (Fig. 5). Tregs can suppress antitumor responses, leading to tumor immune escape. DCs can promote tumor metastasis by increasing Treg cells and decreasing the cytotoxicity of CD8 + T cells [20–23]. Previous studies have also proven that the proportion of macrophages, CD8 + T cells, Tregs, and MDSCs in BC patients correlates with poor prognosis [23]. These results may explain why low expression of CLEC10A partly affects the prognosis of BC patients through immune infiltration.

In this study, we first reported that low expression of CLEC10A was significantly associated with poor survival and immune infiltration in BC patients through bioinformatic analysis. CLEC10A may be regarded as a potential new biomarker to predict treatment outcomes in BC. Furthermore, our study

provides new and promising insight for further elucidating significant clinicopathological factors and molecular pathogenesis mechanisms of BC. The mechanism by which CLEC10A promotes BC progression will be verified in further studies.

## Abbreviations

CLEC10A: C-type lectin domain family 10, member A; BC:Breast cancer; TIMER:The Tumor Immune Estimation Resource; TCGA:The Cancer Genome Atlas; OS:Overall survival; PFI:Progression-free interval; HR:Hazard ratio; CIs:Confidence intervals; DFS:Disease-free survival.

## Declarations

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We thank all of the participants for their participation and The Xiantao platform.

### Author's contributions

FFC designed and managed the entire study; SST and ZY downloaded and analyzed the data and wrote the main manuscript text; XYL, CMC, LYY and HYZ wrote and revised the manuscript; All authors read and approved the final manuscript.All authors contributed to the article and approvedthe submitted version

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### Availability of data and materials

The datasets used and/or analyzed during the current study are available fromthe TCGA.

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Competing interests

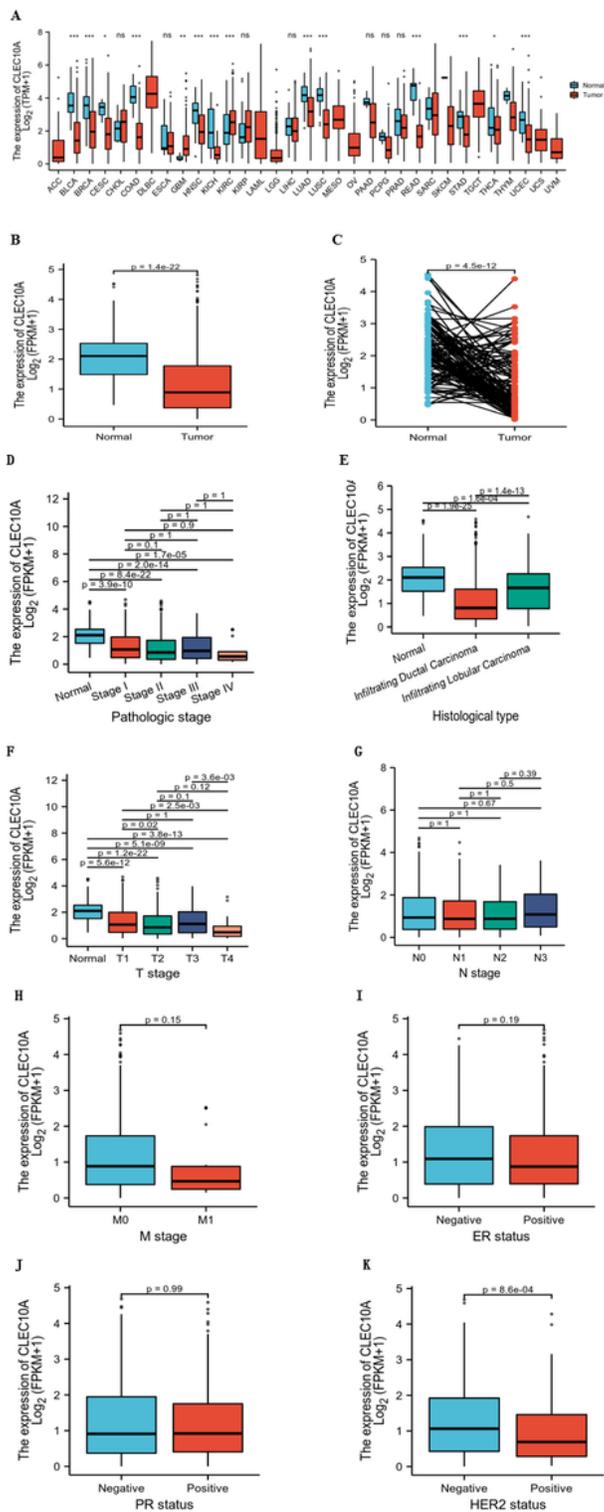
The authors declare that they have no competing interests.

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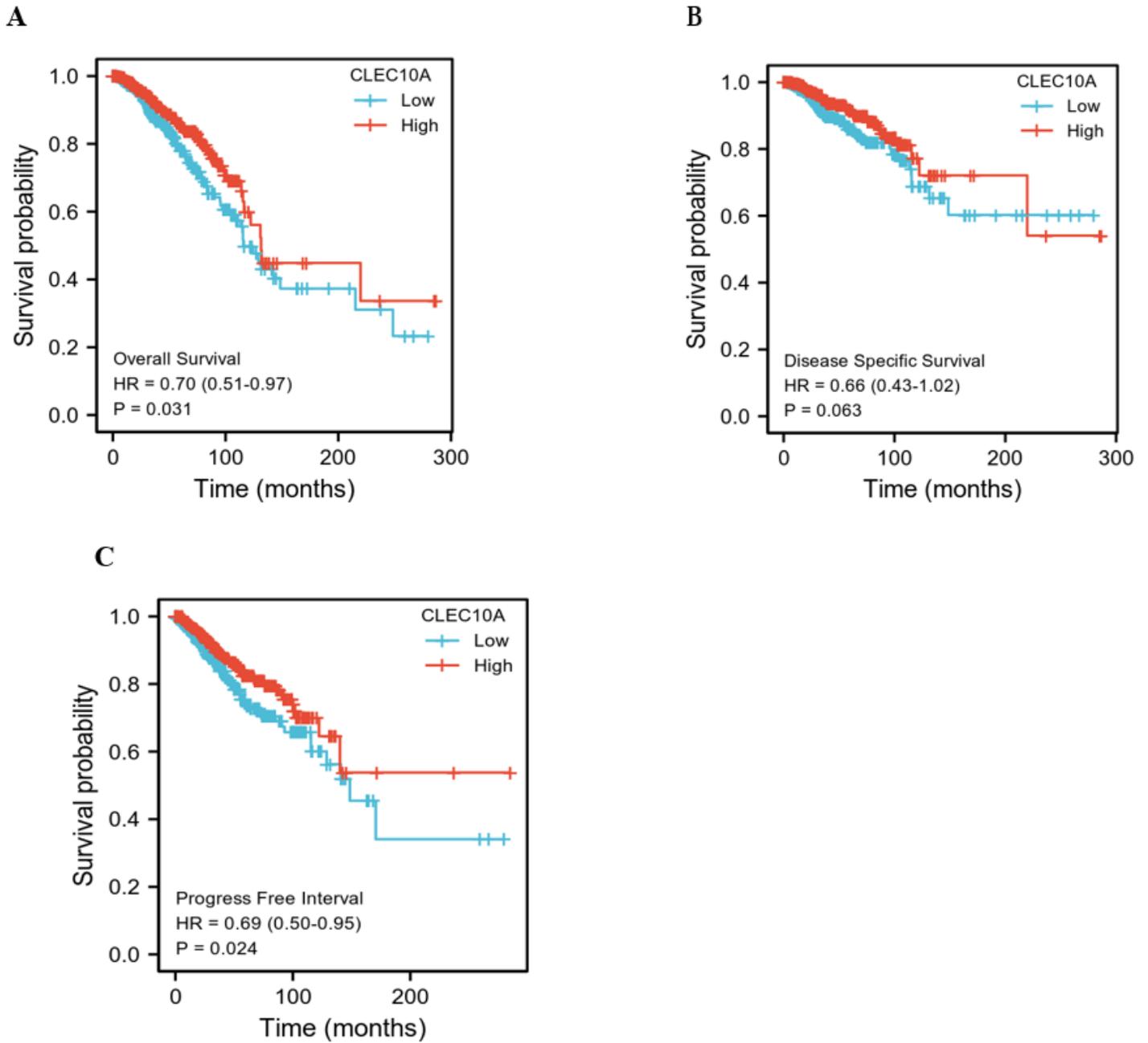
## Figures



**Figure 1**

The expression of CLEC10A in different cancers and its relationship with individual clinical parameters of BC. (A) CLEC10A mRNA expression level in different cancers tissues compared to normal tissues in TIMER database. (B) CLEC10A expression difference in BC non-paired samples. (C) CLEC10A expression difference in BC paired samples. (D–F) CLEC10A mRNA expressions were remarkably correlated with BC

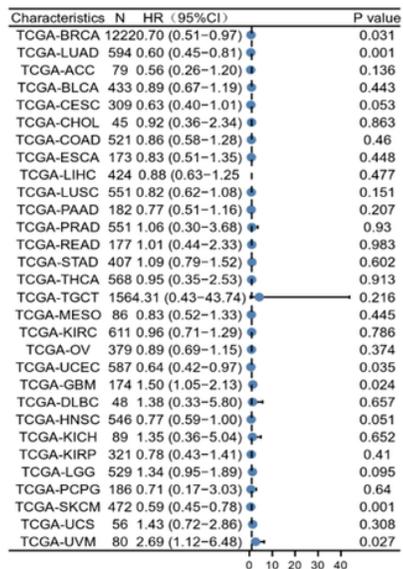
patients' individual cancer pathologic stages (D), histological type (E). T stages (F), N stages. (G), metastasis stage (H), ER status (I). PR status (J). HER2 status(K). \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ .



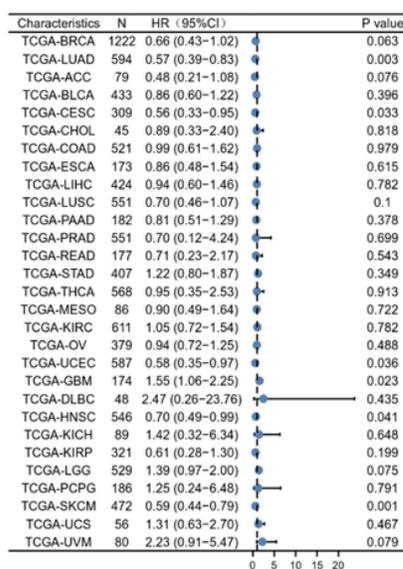
**Figure 2**

Comparison of Kaplan-Meier survival curves of CLEC10A high and low expression in breast cancers. (A, C) Low CLEC10A expression had poor OS and PFI in BC.

A



B



C

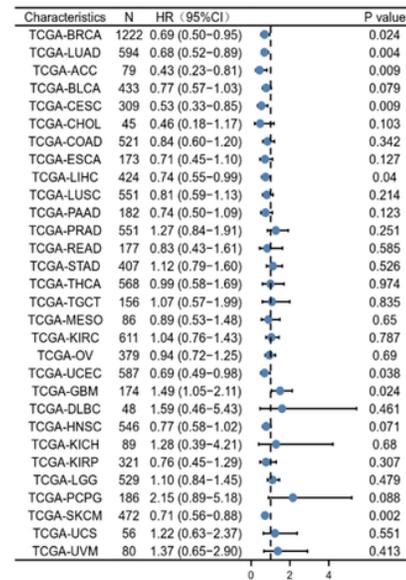
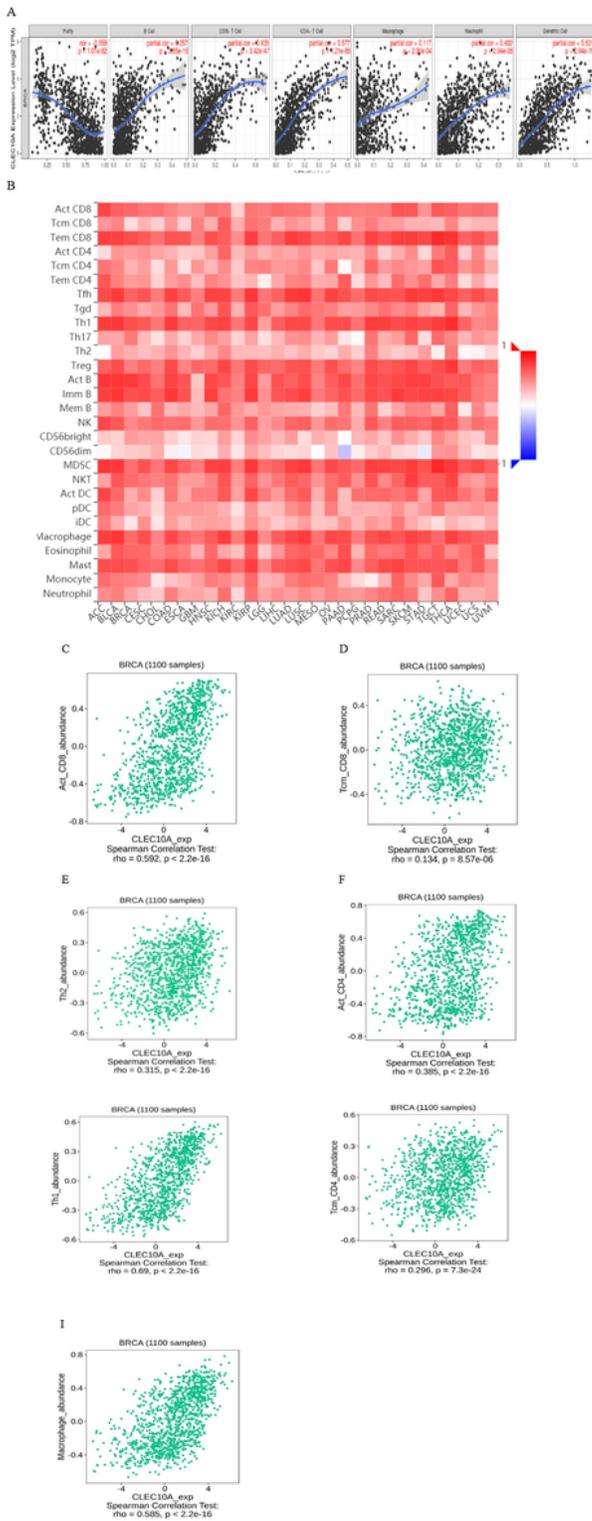


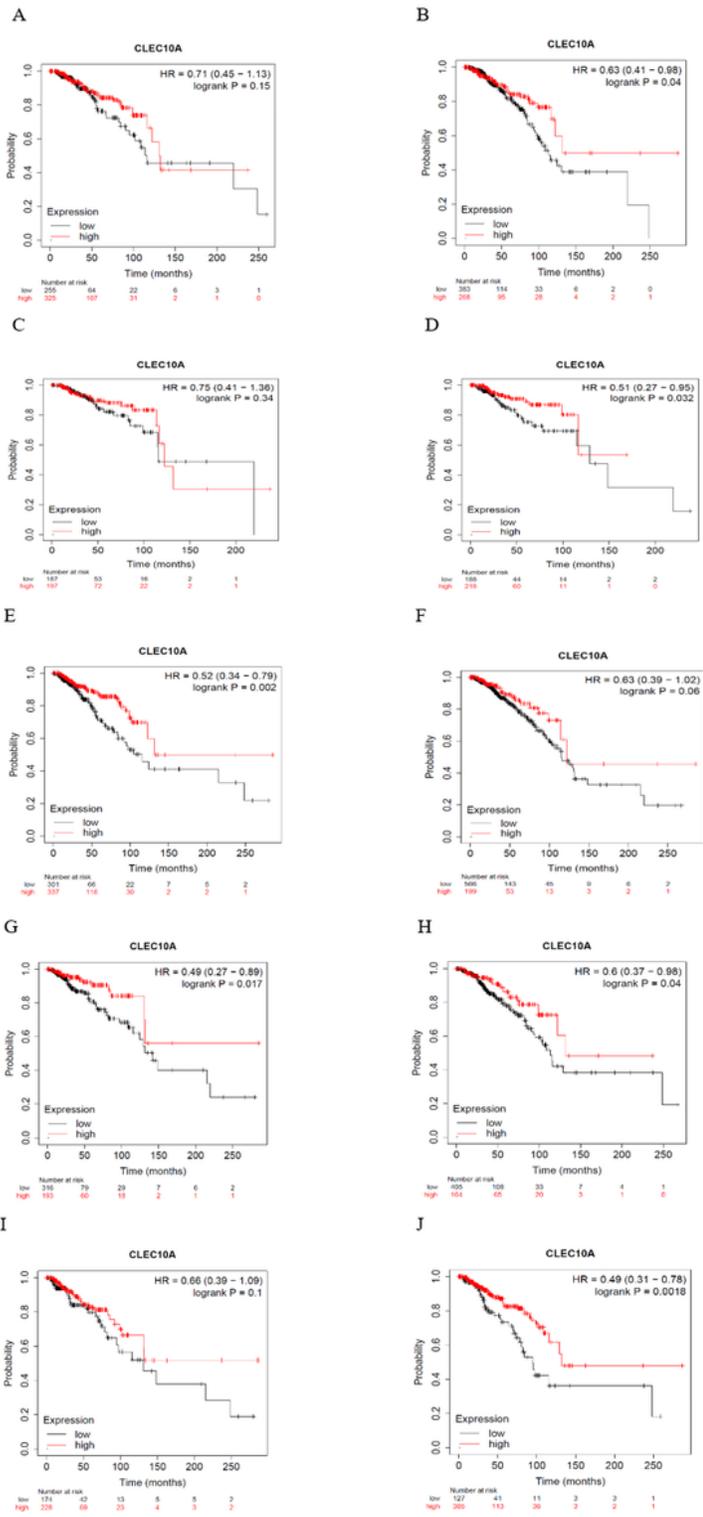
Figure 3

Forest plot of the prognostic values in BC of CLEC10A. (A-C) Prognostic HR of CLEC10A in BC for OS (A), DSS (B), PFI (C).



**Figure 4**

Correlation analysis of CLEC10A level and immune cells infiltration levels in BC using the TIMER database and TISIDB database. (A) CLEC10A expression in BC tissues positive correlates with tumor immune infiltration levels of B cells, CD8+ T cells, CD4+ T cells, macrophage, neutrophils, and dendritic cells. (B) Relations between expression of CLEC10A and 28 types of TILs across human heterogeneous cancers. (C-J) TILs were displaying the greatest Spearman's correlation with CLEC10A expression in BC.



**Figure 5**

Comparison of Kaplan-Meier survival curves of the high and low expression of CLEC10A in BC based on immune cells subgroups. (A–G) Low CLEC10A level enriched in B cells, CD4+ memory T cells, CD8+ T cells, macrophages, NK T cells, Treg T cells, Th1 cells had worse OS in BC.