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Original Article

Upregulated PXDNL promotes invasive breast carcinoma progression

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Abstract: Background: Invasive breast carcinoma (BRCA) is a common and serious malignancy in women. Peroxidase-like (PXDNL) is associated with poor prognosis in various cancers but has an unclear role in BRCA progression. Methods: Bioinformatic analysis of datasets from The Cancer Genome Atlas (TCGA), Genotype-Tissue Expression (GTEx), and UALCAN investigated a potential carcinogenic role of PXDNL, focusing on its correlation with prognosis, promoter methylation, immune cell infiltration, immune checkpoint genes, and relevant biologic functions and pathways. Results: PXDNL demonstrated a significant expression profile in BRCA, with considerable diagnostic and prognostic implications. Its up-regulation correlated with decreased survival rates across various molecular subtypes of BRCA. Patients in the high PXDNL expression group showed reduced presence of multiple infiltrative immune cell types, including CD8+ T cells, cytotoxic cells, T cells, B cells, dendritic cells (DC), immature dendritic cells (iDC), natural killer (NK) cells, NK CD56bright cells, NK CD56dim cells, and follicular helper T cells (TFH). Additionally, a significant correlation was observed between PXDNL expression and immune checkpoint genes. Gene Set Enrichment Analysis (GSEA) further indicated that high PXDNL expression triggers pathways such as epithelial-mesenchymal transition and protein secretion, while suppressing crucial processes including allograft rejection, IL6-JAK-STAT3 signaling, TNFα signaling via NFκB, adipogenesis, oxidative phosphorylation, DNA repair, and the P53 pathway. Conclusion: Overexpression of PXDNL is associated with poor prognosis and is linked to immune cell infiltration in BRCA. Thus, PXDNL may be a biomarker or therapeutic target for BRCA.

Keywords: Breast invasive carcinoma, PXDNL, prognosis, immune infiltration, immune checkpoints

Introduction

Invasive breast carcinoma (BRCA) is one of the most prevalent malignant tumors in women worldwide [1, 2]. According to the World Health Organization (WHO), there were more than 2.3 million new cases of BRCA worldwide in 2022, accounting for 11.6% of all cancer cases, and it is a leading cause of cancer-related death in women [3]. In recent years, significant progress has been made in the treatment of BRCA. The combined use of multiple therapies, including surgical resection, chemotherapy, radiotherapy, endocrine therapy and molecularly targeted therapies has significantly improved the prognosis [4]. For example, endocrine therapy (e.g. tamoxifen and aromatase inhibitors) for hormone receptor (HR) positive BRCA significantly reduced the risk of recurrence [5]; and targeted therapies (e.g. trastuzumab) for human epidermal growth factor receptor 2 (HER2) positive BRCA significantly improved patient survival [6]. However, certain patients, such as those with triple-negative breast cancer, remain at high risk of recurrence and metastasis due to tumor heterogeneity and lack of effective therapeutic targets [7, 8]. In addition, although immune checkpoint inhibitors (e.g. PD-1/PD-L1 inhibitors) have shown favorable efficacy in some BRCA patients, some patients still face the risk

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of recurrence, metastasis and death [9, 10]. Therefore, in-depth research into the pathogenesis of BRCA to identify new specific biomarkers is crucial for assessing prognosis and guiding treatment in BRCA.

Peroxidasin-like (PXDNL) belongs to the peroxidase gene family, with molecular functions including nuclease activity, peroxidase activity and protein binding [11, 12]. PXDN is an important paralog of PXDNL. PXDNL exists in three isoforms (164, 147 and 57-kDa) produced by alternative splicing [11]. The 57-kDa isoform is distributed in the cytoplasm of several human tumor cell lines (MCF-7, MDA, U2OS, 293T and K562) and has been confirmed to be the only variable splicing product of PXDNL in these tumor cells [13]. PXDNL is strongly associated with several cancer diagnoses and prognosis. Previous studies have found that PXDNL is highly expressed in BRCA samples and is associated with a poorer prognosis [14]. Furthermore, in 6697 patients with BRCA, a cohort study found that the top driving oncogenes, including PXDNL, had a mutation prevalence of > 5% [15]. However, the specific role of PXDNL in BRCA has not yet been elucidated.

In this study, we analyzed the expression level of PXDNL in BRCA. To explore in detail the possible mechanisms of PXDNL expression in BRCA, BRCA samples were obtained from public databases. Then, the correlation between PXDNL and clinicopathologic features and their clinical significance were investigated to determine the prognostic value of PXDNL in BRCA. In addition, the molecular mechanisms in BRCA were investigated by probing the relationship between PXDNL, immune cell infiltration and immune checkpoints. Finally, functional enrichment analysis was used to identify the relevant functional pathways of PXDNL in BRCA tumor development and progression.

Materials and methods

Data acquisition and processing

The transcriptome expression data together with corresponding clinicopathologic information were acquired from The Cancer Genome Atlas (TCGA) database (http://cancergenome.nih.gov) and Genotype-Tissue Expression (GTEx) database (http://commonfund.nih.gov/GTEx/). Moreover, ULCAN database (http://ualcan.path.uab.edu/) was used to analyze differential methylation of PXDNL in TCGA-BRCA samples and normal tissues [16].

Diagnostic and prognostic analysis

The diagnostic and prognostic value of PXDNL in BRCA was determined using the mRNA expression data of tumor tissues and normal tissues from TCGA. The receiver operating characteristic (ROC) curve was used for this analysis and performed by the "pROC" R package [17, 18], and the results were plotted using the "ggplot2" R package. An area under the curve (AUC) value was then calculated to evaluate the ROC effect.

Survival analysis and clinicopathologic characteristics analysis

The correlation between PXDNL and pan-cancer overall survival (OS) was assessed using Cox regression and presented in forest plots. According to the optimal cut-off value of PXDNL, BRCA samples in TCGA were classified into high-expression and low-expression groups. Kaplan-Meier (KM) survival analysis was then performed on all BRCA patients to assess the difference in OS, disease specific survival (DSS), and progression free interval (PFI) between the two groups. Subsequently, KM survival analyses were performed in BRCA patients with three different molecular markers: ER, progesterone receptor (PR), and HER2, to assess the differences in OS between high and low PXDNL expression groups. The "Survival" and "survminer" packages were used for statistical analysis and visualization, respectively. In addition, correlations between expression and clinicopathologic features such as age, race, PAM50 and different molecular markers were explored based on clinical information of BRCA patients collected in the TCGA database.

Immune cell infiltration and immune checkpoints

Single-sample Gene Set Enrichment Analysis (ssGSEA) was used to calculate the relative abundance of different immune cell types [19, 20]. The correlation between PXDNL expression and immune cell infiltration was examined using the Spearman correlation coefficient. Additionally, we examined the relationship between PXDNL expression and immune checkpoints.

Differential analysis of expressed genes

Using R package "limma" [21], we identified the differentially expressed genes (DEGs) between the high PXDNL expression group and low PXDNL expression group. |Log2 Fold change (FC)| > 0.5 and adjusted P value < 0.05 were set as the cut-offs to screen for DEGs. Results were shown by volcano plot.

Functional analysis

Functional enrichment analysis of DEGs was performed by R package "clusterProfiler" to identify Gene Ontology (GO) categories by their biological processes (BP), cellular components (CC), or molecular functions (MF). R package "clusterProfiler" was also used to perform Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways [22]. Furthermore,Gene Set Enrichment Analysis (GSEA) was performed on HALLMARK terms to characterize biologic functions and pathways related to PXDNL [23]. The mountain range diagram lists the top HALLMARK terms.

Enzyme-linked immunosorbent assay (ELISA)

Serum samples were collected from 27 healthy individuals and 47 BRCA patients from the Affiliated Bozhou Hospital of Anhui Medical University. According to the guidelines given by the manufacturer, the optical density (OD) was measured at 450 nm using a microplate reader. A standard curve was then used to determine the concentration of PXDNL in each sample. This study was approved by the Medical Ethics Committee of the Affiliated Bozhou Hospital of Anhui Medical University.

Statistical analysis

Statistical analyses were performed by R software (version 4.2.1). The Wilcoxon test was used to assess the difference in PXDNL expression between the two groups. KM curves reflected the prognosis of PXDNL expression on the survival of BRCA patients. Spearman analysis was performed to calculate correlation coefficients. P < 0.05 was considered significant.

Results

Expression levels of PXDNL

Differences in PXDNL expression levels between tumor tissues and adjacent normal tissues in the TCGA database were first explored. As shown in **Figure 1A**, the mRNA expression of PXDNL was significantly increased in BRCA, cholangiocarcinoma (CHOL), esophageal carcinoma (ESCA), glioblastoma multiforme (GBM), head and neck squamous cell carcinoma (HNSC), liver hepatocellular carcinoma (LIHC), pheochromocytoma and paraganglioma (PCPG), and stomach adenocarcinoma (STAD). Conversely, decreased PXDNL expression was observed in kidney chromophobe (KICH), kidney renal papillary cell carcinoma (KIRP), prostate adenocarcinoma (PRAD), and thyroid carcinoma (THCA). Due to the lack of corresponding normal tissue expression data in the TCGA database, matching normal tissue expression data from the GTEx database were further obtained for merged analysis. As visible in **Figure 1B**, PXDNL expression was elevated in most cancers, including adrenocortical carcinoma (ACC), bladder urothelial carcinoma (BLCA), BRCA, CHOL, diffuse large B-cell lymphoma (DLBC), GBM, HNSC, kidney renal clear cell carcinoma (KIRC), acute myeloid leukemia (LAML), LIHC, lung adenocarcinoma (LUAD), lung squamous cell carcinoma (LUSC), ovarian serous cystadenocarcinoma (OV), pancreatic adenocarcinoma (PAAD), PCPG, skin cutaneous melanoma (SKCM), STAD, thymoma (THYM) and uterine carcinosarcoma (UCS). In contrast, PXDNL expression in the tumor tissues of cervical squamous cell carcinoma (CESC), colon adenocarcinoma (COAD), KIRP, lower grade glioma (LGG), PRAD, rectum adenocarcinoma (READ) and testicular germ cell tumors (TGCT) was significantly decreased.

Subsequently, we further validate the expression of PXDNL in BRCA. The results revealed that PXDNL expression was significantly upregulated in BRCA tissues compared to normal tissues in both the TCGA and TCGA-GTEx cohorts (**Figure 2A**, **2B**). Moreover, high expression of PXDNL was also confirmed in 113 paired BRCA tissues (**Figure 2C**).

In addition, ROC curve analysis was performed to further explore the diagnostic and prognostic value of PXDNL in BRCA. Based on the TCGA cohort, the AUC value of the diagnostic ROC curve for PXDNL was 0.616 (**Figure 2D**). The prognostic AUC values for PXDNL at 1, 3, 5 years were 0.624, 0.628, and 0.630, respectively (**Figure 2E**). Furthermore, we used the UALCAN database to identify differences in pro-

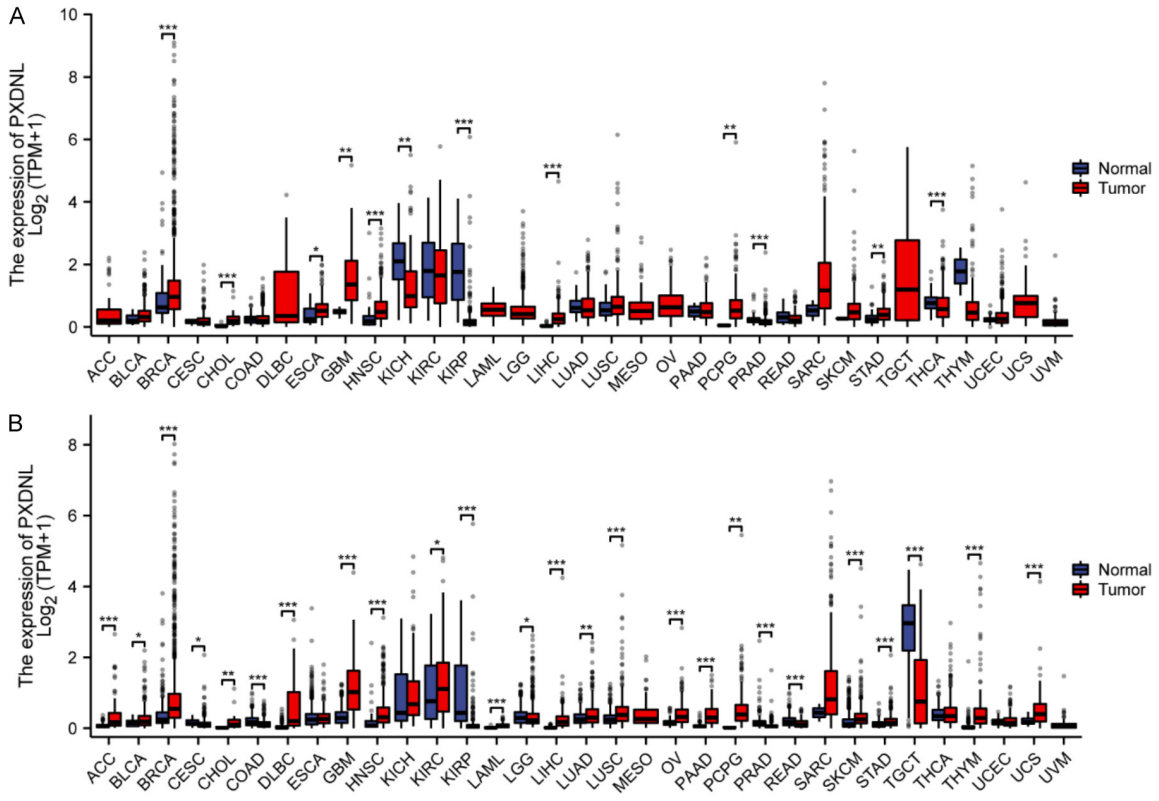

Figure 1. Peroxidasin like (PXDNL) expression in pan-cancer. A. Comparison of PXDNL expression between tumor and paracancerous tissues across 33 cancers in The Cancer Genome Atlas (TCGA) database. B. Comparison of PXDNL expression between tumor and normal tissues across 33 cancers in TCGA and the Genotype-Tissue Expression (GTEx) database. *P < 0.05, **P < 0.01, ***P < 0.001.

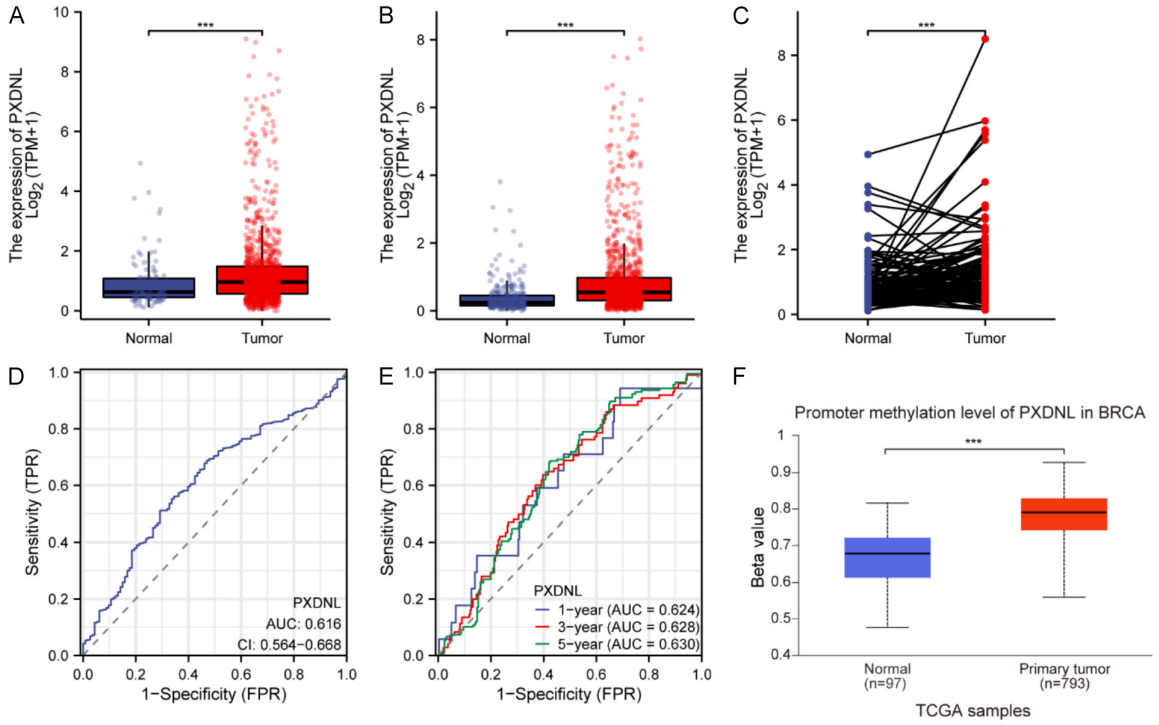

Figure 2. Relationship between PXDNL expression and invasive breast carcinoma (BRCA). A. Differential expression of PXDNL between tumor tissues and paracancerous tissues in TCGA. B. Differential expression of PXDNL between tumor tissues and normal tissues in TCGA and GTEx. C. Differential expression of PXDNL between tumor tissue and matched paracancerous tissue. D. Diagnostic receiver operating characteristic (ROC) curve of PXDNL in BRCA. E. 1, 3, 5 year prognostic ROC curves of PXDNL in BRCA. F. Promoter methylation levels of PXDNL in BRCA. ***P < 0.001.

moter methylation levels of PXDNL in BRCA. As illustrated in **Figure 2F**, promoter methylation levels of PXDNL were elevated in BRCA tissues compared to normal tissues in the TCGA cohort.

PXDNL expression correlates with cancer survival and prognosis

To further elucidate the effect of PXDNL expression on the prognosis of cancer patients, we used Cox regression analysis to explore the relationship between PXDNL expression and OS in 33 cancers. As presented in **Figure 3A**, high PXDNL expression was significantly associated with poorer prognosis in BLCA, BRCA, COAD, KIRP, and LGG. Subsequently, the relationship between PXDNL expression and prognosis in BRCA patients was further analyzed. KM survival curves showed that high PXDNL expression was significantly associated with poorer OS, DSS, and PFI (**Figure 3B-D**). Furthermore, we analyzed the prognostic differences between high and low PXDNL expression groups in patients with different subtypes of BRCA. High PXDNL expression in ER positive, PR positive, PR negative, HER2 positive, and HER2 negative patients indicated a poorer prognosis, whereas PXDNL expression had no prognostic significance in ER negative patients (**Figure 3E-J**).

PXDNL expression is related to clinicopathologic characteristics in BRCA

To shed light on the role of PXDNL in BRCA, the association between PXDNL expression and clinicopathologic characteristics was explored based on clinical information of BRCA patients collected in the TCGA database. BRCA patients were divided into several subgroups based on age, race, PAM50 and different molecular markers. PXDNL expression was higher in BRCA patients with age > 60 years old (**Figure 4A**). Additionally, PXDNL expression was higher in White BRCA patients and lower in Black or African American BRCA patients (**Figure 4B**). Notably, PXDNL expression varied across different BRCA subtypes (Basal, Luminal-A (LumA), Luminal-B (LumB), and HER2). Among these subtypes, PXDNL expression was higher in Basal and LumB subtypes, while the lowest expression was observed in HER2 patients (**Figure 4C**). However, no significant differences in PXDNL expression were found between BRCA patients with different molecular markers (**Figure 4D-F**).

PXDNL and the immune microenvironment in BRCA

The proportions of 24 different immune cell types were estimated using ssGSEA. ssGSEA analyses showed that PXDNL expression was significantly and positively correlated with macrophages, Th2 cells, gamma-delta T cells (Tgd), and central memory T cells (Tcm), while it was negatively correlated with CD8 T cells, cytotoxic cells, T cells, B cells, dendritic cells (DC), interdigitating DC (iDC), natural killer (NK) cells, NK CD56bright cells, NK CD56dim cells, and follicular helper T cells (TFH) (**Figure 5A**, **5B**).

Given that immunotherapy targeting immune checkpoints represents an emerging field in BRCA treatment, the relationship between PXDNL expression and immune checkpoint genes in BRCA patients was explored. It was observed that genes HAVCR2, TNFSF18, CD276, CD86, TNFSF4, and CD160 were more highly expressed in the high-expression group, suggesting that immunotherapy may be beneficial for this high-risk group (**Figure 5C**).

Identification of DEGs in BRCA and functional enrichment analysis

To further elucidate the mechanism of PXDNL in BRCA, we categorized BRCA patients into high and low expression groups based on the median expression level of PXDNL. In total, we identified 1209 DEGs, including 611 up-regulated and 598 down-regulated DEGs, with an adjusted P value < 0.05 and |Log2 FC| > 0.5 (**Figure 6A**). Moreover, **Figure 6B** shows the association between PXDNL and the top 10 DEGs (CSN2, SULT1C3, SMR3B, LCE1A, CSN1S1, FGF4, CYP2A6, PRB2, NCAN and PRB1).

A PXDNL – Overall Survival

Group	Total(N)	HR(95% CI)	P value
ACC	79	0.916 (0.436 – 1.927)	0.8177
BLCA	411	1.430 (1.065 – 1.919)	0.0174
BRCA	1086	1.811 (1.305 – 2.513)	0.0004
CESC	306	1.247 (0.785 – 1.983)	0.3499
CHOL	35	0.999 (0.379 – 2.629)	0.9979
COAD	477	1.509 (1.019 – 2.236)	0.0401
DLBC	48	0.504 (0.110 – 2.302)	0.3766
ESCA	163	1.021 (0.627 – 1.662)	0.9334
GBM	168	1.024 (0.726 – 1.443)	0.8945
HNSC	503	0.902 (0.690 – 1.180)	0.4535
KICH	64	1.135 (0.304 – 4.230)	0.8508
KIRC	541	0.828 (0.615 – 1.114)	0.2121
KIRP	290	2.147 (1.143 – 4.032)	0.0175
LAML	139	1.284 (0.840 – 1.964)	0.2478
LGG	530	2.077 (1.451 – 2.972)	6.5e−05
LIHC	373	1.199 (0.848 – 1.696)	0.3053
LUAD	530	1.079 (0.810 – 1.438)	0.6034
LUSC	496	1.233 (0.940 – 1.619)	0.1306
MESO	86	1.054 (0.663 – 1.675)	0.8239
OV	379	1.033 (0.799 – 1.336)	0.8040
PAAD	179	1.430 (0.950 – 2.153)	0.0865
PCPG	184	0.686 (0.160 – 2.940)	0.6121
PRAD	501	1.175 (0.334 – 4.135)	0.8019
READ	166	0.875 (0.404 – 1.895)	0.7356
SARC	263	1.211 (0.816 – 1.799)	0.3422
SKCM	457	1.184 (0.902 – 1.555)	0.2230
STAD	370	1.028 (0.741 – 1.427)	0.8679
TGCT	139	0.429 (0.043 – 4.261)	0.4701
THCA	512	2.044 (0.710 – 5.884)	0.1853
THYM	119	1.815 (0.447 – 7.371)	0.4043
UCEC	553	1.451 (0.964 – 2.186)	0.0745
UCS	57	0.652 (0.328 – 1.297)	0.2229
UVM	80	2.338 (0.988 – 5.533)	0.0534

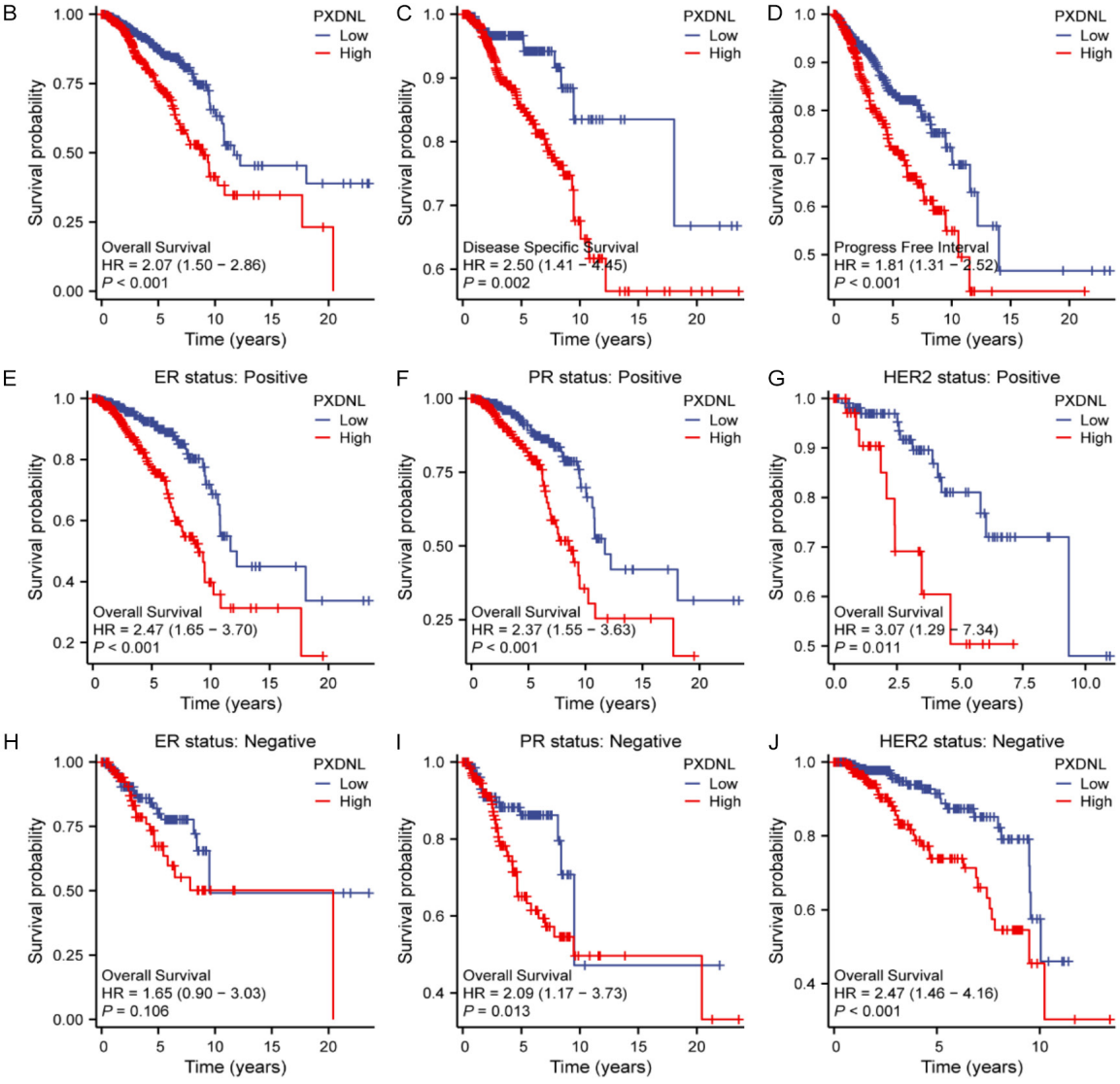

Figure 3. Prognostic significance of PXDNL in pan-cancer and BRCA. (A) In the TCGA database, forest plots illustrate the relationship between PXDNL expression and patient overall survival (OS) for pan-cancer. (B-D) Kaplan-Meier (KM) curves display that PXDNL expression correlated with OS, disease specific survival (DSS) and progression free interval (PFI) in BRCA. KM curves show the relationship between PXDNL expression and OS in patients with different molecular subtypes of BRCA, including (E) Estrogen receptor (ER) positive, (F) Progesterone receptor (PR) positive, (G) Human epidermal growth factor 2 (HER2) positive, (H) ER negative, (I) PR negative, (J) HER2 negative.

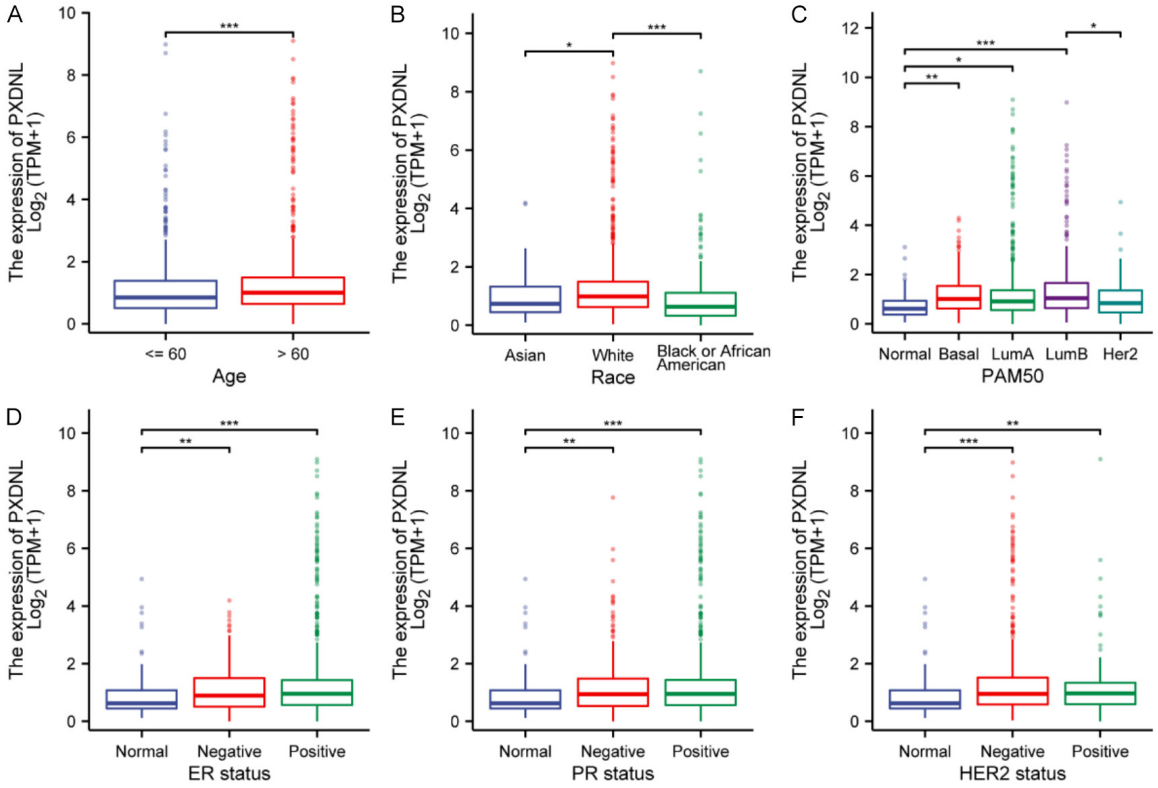

Figure 4. Correlation between PXDNL expression and clinical characteristics. Association of PXDNL expression with (A) age, (B) race, (C) PAM50, (D) ER status, (E) PR status, (F) HER2 status. *P < 0.05, **P < 0.01, ***P < 0.001.

Next, these DEGs were analyzed for functional and pathway enrichment. Results show that in GO terms these DEGs were mainly related to sensory perception of bitter taste, detection of chemical stimulus involved in sensory perception of bitter taste, antimicrobial humoral response, chemokine-mediated signaling pathway, humoral immune response, integral component of synaptic membrane, intrinsic component of synaptic membrane, integral component of postsynaptic membrane, intrinsic component of postsynaptic membrane, collagen-containing extracellular matrix, receptor ligand activity, signaling receptor activator activity, serine-type endopeptidase activity, serine hydrolase activity, and serine-type peptidase activity (**Figure 6C**). The KEGG pathway enrichment analysis revealed that Neuroactive ligand-receptor interaction, Cytokine-cytokine receptor interaction, Viral protein interaction with cytokine and cytokine receptor, Primary immunodeficiency, and IL-17 signaling pathway were enriched in DEGs (**Figure 6C**). In addition, GSEA results showed that processes such as allograft rejection, IL6-Jak-STAT3 signaling, TNFα signaling via NFκB, adipogenesis, oxidative phosphorylation, DNA repair and P53 pathway were negatively correlated with PXDNL expression, while processes such as KRAS signaling downstream, epithelial mesenchymal transition, and protein secretion were positively correlated with PXDNL expression (**Figure 6D**).

PXDNL protein is highly expressed in the serum of BRCA patients

To investigate the diagnostic potential of PXDNL in BRCA patients, serum samples from 27 nor-

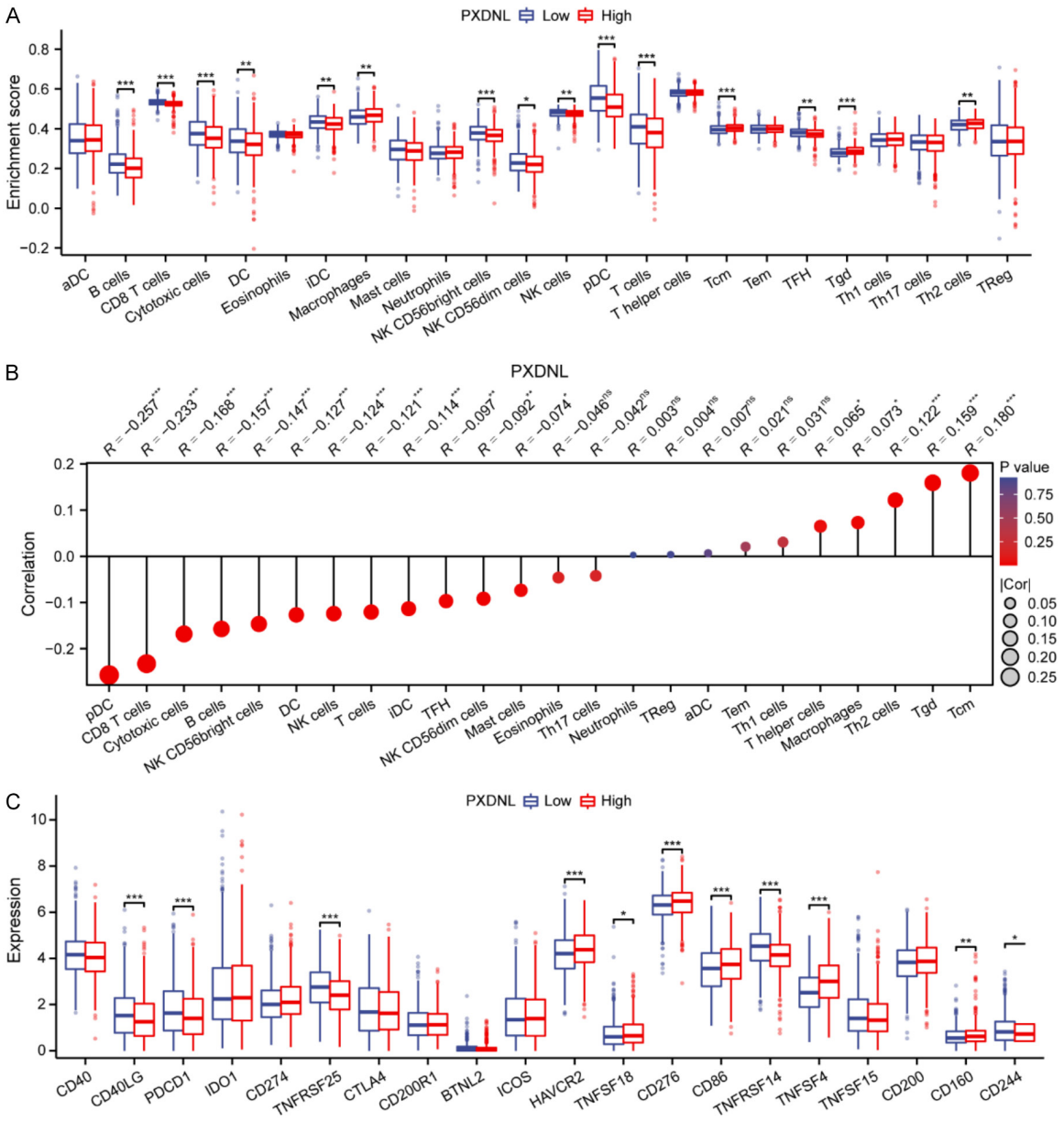

Figure 5. Analysis of immune infiltration and immune checkpoints. A. Differences in immune cell infiltration scores between high and low PXDNL expression groups. B. Relationship between PXDNL expression and immune cells. C. Differences in immune checkpoint gene expression between high and low PXDNL expression groups. *P < 0.05, **P < 0.01, ***P < 0.001.

mal controls and 47 BRCA patients were collected for ELISA analysis. The results revealed significantly elevated serum PXDNL levels in BRCA patients (**Figure 7A**), consistent with the high expression levels observed in the TCGA and GTEx databases. Notably, in **Figure 7B**, PXDNL expression was lower in ER, PR negative, and HER2 positive BRCA patients. In contrast, as shown in **Figure 7C** PXDNL expression was higher in ER, PR, and HER2 strongly positive BRCA patients.

Discussion

Breast carcinoma (BRCA) is a heterogeneous disease with high morbidity. Molecular subtype classifications have deepened our understanding of BRCA and can guide BRCA treatment. Despite significant improvement in BRCA therapy, many patients remain refractory or experience recurrence after treatment. Therefore, it is vital to identify new clinical biomarkers and therapeutic targets that will benefit BRCA pa-

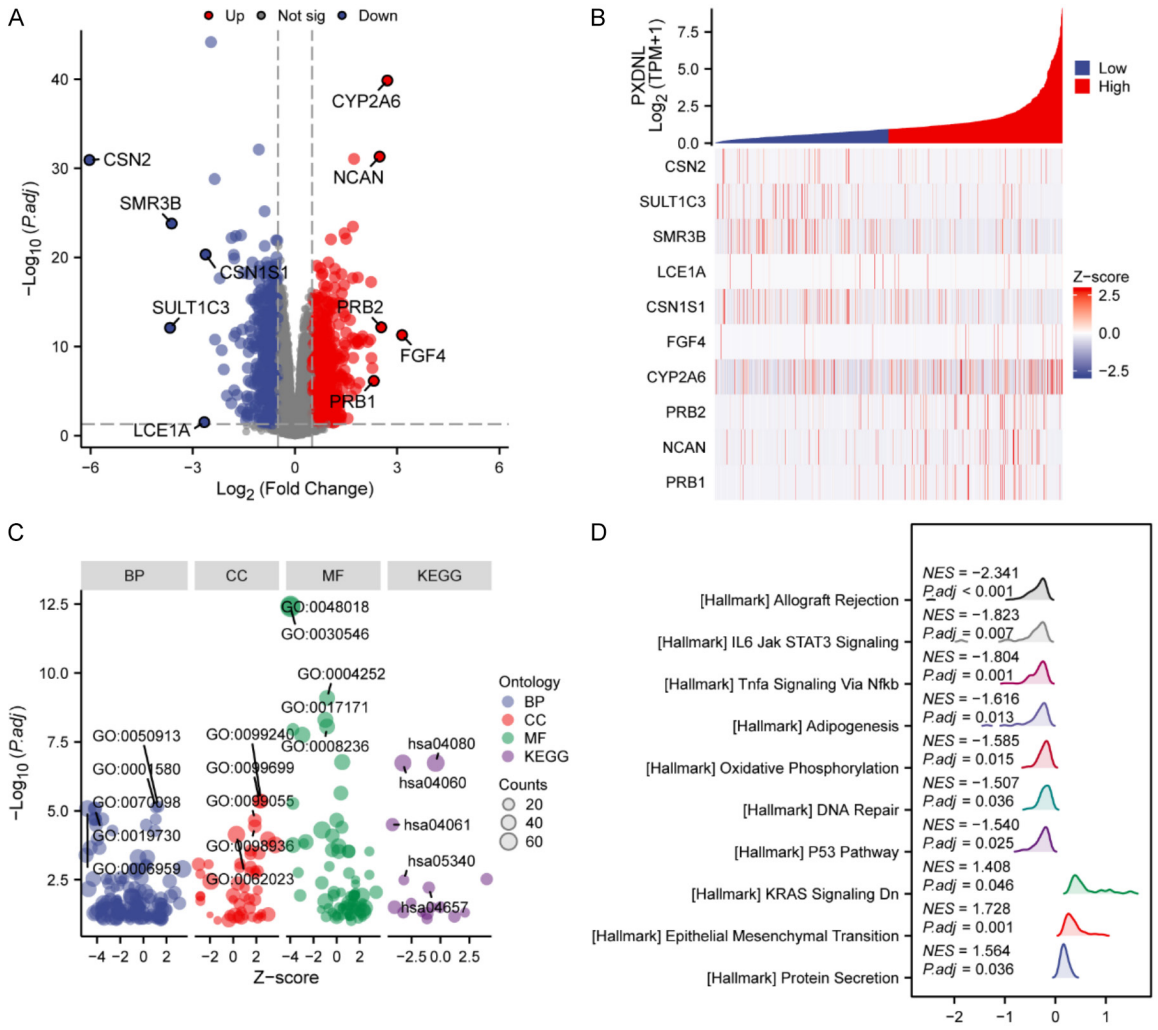

Figure 6. Differential gene identification and functional enrichment analysis. A. Volcano plot of the differentially expressed genes (DEGs), and the top 10 genes with the highest differences were marked. B. Top 10 genes of correlated with PXDNL were shown in Heatmap. C. Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis of DEGs (|Log2 Fold change (FC)| > 0.5, adjusted P-value < 0.05). D. Gene Set Enrichment Analysis (GSEA) enrichment analysis of DEGs.

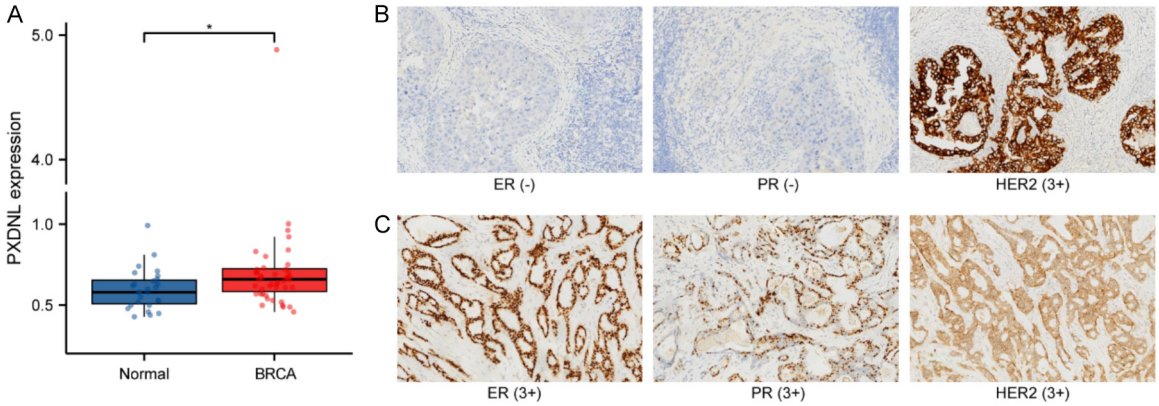

Figure 7. PXDNL protein expression in serum of BRCA patients. A. Differences in PXDNL protein expression in serum of normal controls and BRCA patients. B. PXDNL protein levels in ER, PR negative, and HER2 positive BRCA patients. C. PXDNL protein levels in ER, PR and HER2 strongly positive BRCA patients. *P < 0.05.

tients. In this study, the TCGA and GTEx datasets were used to demonstrate that PXDNL is upregulated in BRCA compared to adjacent normal tissue. Analysis of clinical samples further validated this result. Subsequently, through ROC and survival analyses, we determined that high expression of PXDNL showed higher diagnostic and prognostic effects in patients with different molecular subtypes of BRCA.

The tumor microenvironment (TME), composed of tumor cells, immune cells and cytokines, interacts with each other and plays a crucial role in tumor progression, patient prognosis, and immunotherapy [24-26]. By analyzing immune cell infiltration in TME, we found that most immune cells were significantly insufficient in the high PXDNL expression group, such as CD8 T cells, cytotoxic cells, T cells, B cells, DC, iDC, NK cells, NK CD56bright cells, NK CD56dim cells, and TFH. CD8 T cells and NK cells are major effector immune cells capable of directly killing tumor cells, while B cells and DCs are essential for antigen presentation and immune activation. The reduction of these cells in the high PXDNL expression group may weaken the anti-tumor immune response, thereby promoting tumor immune escape [27]. However, macrophages, Th2 cells, Tgd, and Tcm were significantly higher in the high PXDNL expression group. Macrophages, in different activation states (M1, M2), have anti-tumor and pro-tumor effects, respectively [28]. High expression of PXDNL may alter macrophage polarization and function, increasing the proportion of M2 macrophages and thereby promoting the formation of an immunosuppressive TME. Additionally, Th2 cell infiltration is closely associated with tumor growth and immunosuppressive functions [29]. Th2 cells secrete cytokines such as IL-4, IL-5, and IL-13, which suppress the anti-tumor immune responses and activate cancer-associated fibroblasts, further exacerbating the immunosuppressive state of the TME. In addition, high expression of PXDNL was associated with the upregulation of several immune checkpoint genes, and PXDNL may further promote the formation of immunosuppressive TME by modulating immune checkpoints, and may also affect the efficacy of immunotherapy. In conclusion, the high expression of PXDNL may promote the formation of immunosuppressive TME through multiple mechanisms, which together weaken the anti-tumor immune response of the body and create favorable conditions for tumor progression and immune escape.

To elucidate the mechanism of actions of PXDNL in BRCA, genes associated with PXDNL expression were evaluated by differential gene expression, and these DEGs were subjected to functional enrichment analyses. GO enrichment analysis indicated that PXDNL may be involved in several cellular immune functions, synaptic compositions, and enzyme activity regulation. KEGG pathway analysis revealed that PXDNL significantly negatively regulated neuroactive ligand-receptor interactions, cytokine-cytokine receptor interactions, viral proteins interacting with cytokines and cytokine receptors, primary immunodeficiency, and the IL-17 signaling pathway. Moreover, GSEA results revealed that PXDNL expression activated processes such as epithelial-mesenchymal transition and protein secretion, whereas processes such as allograft rejection, IL6 Jak-STAT3 signaling, TNFα signaling via NFκB, adipogenesis, oxidative phosphorylation, DNA repair, and the P53 pathway were inhibited. These findings suggest that PXDNL plays a multifaceted role in BRCA, involving immune regulation, cell signaling, and also affecting the metabolism, migration and metastatic of tumor cells. PXDNL may contribute to tumor growth and metastasis by regulating several key biological processes and signaling pathways.

Based on the analysis of public databases and the validation of clinical serum samples, this study revealed the expression and prognostic role of PXDNL in BRCA. In follow-up work, further biological function experiments are warranted to fully explore the mechanisms and clinical applications of PXDNL in BRCA.

Conclusions

PXDNL is overexpressed in BRCA and is associated with poor prognosis. Its expression level correlates with clinicopathologic features of BRCA patients. In addition, considering the immune cell infiltration and biological functions, PXDNL may become a promising novel prognostic biomarker for BRCA.

Competing interests

The authors declare that the research was conducted in the absence of any commercial or

financial relationships that could be construed as a potential conflict of interest.

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Disclosure of conflict of interest

None.

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