Role of CCND1 Expression in Tumor Immune Microenvironment Modulation and Drug Response in Diffuse large B cell lymphoma: Bioinformatics Approaches

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Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common aggressive non-Hodgkin's lymphoma (NHL) (1). Thirty to forty percent of DLBCL patients were resistant to the standard R-CHOP regimen or recurrence after remission(2). Previous studies have reported that Cyclin D1 (CCND1) may contributes to the tumor microenvironment remodeling and induce drug resistance in various cancers(3,4).

Objectives

To evaluate the role of CCND1 expression in modulating the tumor immune microenvironment and influencing drug resistance in Diffuse Large B-Cell Lymphoma (DLBCL) through integrative bioinformatics approaches.

Methods

CCND1 expression was analyzed using TCGA-DLBC and GTEx datasets and validated by IHC in the HPA database. Its relationship with tumor-infiltrating immune cells was assessed via CIBERSORT and TIMER. Functional roles in cancer pathways and drug sensitivity were further explored using the GSCALite platform.

Results

CCND1 was significantly overexpressed in DLBCL tissues compared to normal controls ($log_2FC = 3.035$; $p < 0.05$) (Fig 1). CIBERSORT analysis indicated that the DLBCL TME predominantly comprises B cells, $CD8^+$ T cells, and M0/M1 macrophages, collectively representing ~60% of immune infiltrates(Fig 2). CCND1 expression showed a positive correlation with $CD8^+$ T cells ($r = 0.432$, $p < 0.01$) and M1 macrophages ($r = 0.594$, $p < 0.01$) (Fig 3). Additionally, CCND1 was strongly associated with immune checkpoint molecules, including PD-L1 ($r = 0.780$, $p < 0.01$) and PDCD1LG2 ($r = 0.835$, $p < 0.01$) (Table 1). Pathway analysis revealed that CCND1 overexpression is associated with the suppression of cell cycle and apoptotic pathways, while promoting epithelial–mesenchymal transition (EMT) (Fig 4). GSCALite-based drug response analysis demonstrated that high CCND1 expression is linked to resistance against key R-CHOP agents, notably doxorubicin and vincristine (Fig 5).

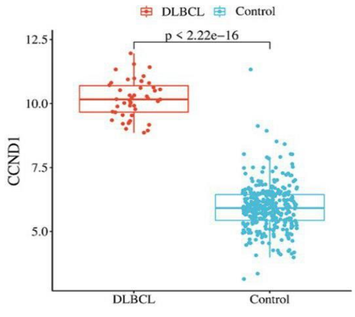


Figure 1. mRNA expression levels of CCND1 in DLBC

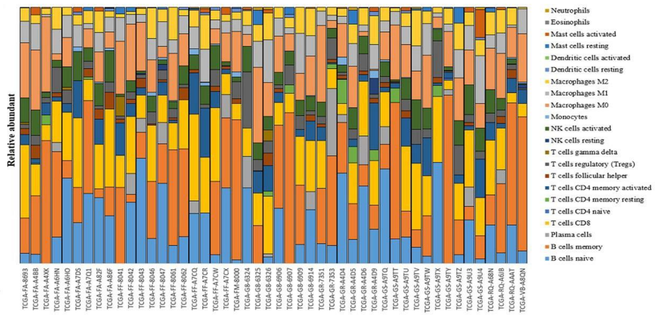


Figure 2. The immune cell fraction in DLBCL

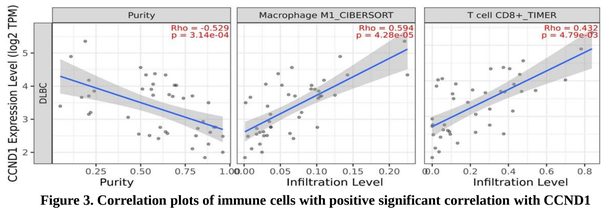


Figure 3. Correlation plots of immune cells with positive significant correlation with CCND1

Table 1. Correlation of CCND1 expression with immune checkpoint molecules

Immune checkpoint	cor	P
PDL1	0.780	p<0.001
PDCD1LG2	0.835	p<0.01

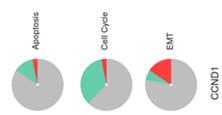


Figure 4. The pathways analysis using GSCALite database

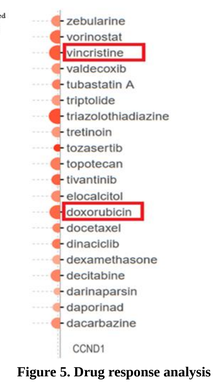


Figure 5. Drug response analysis

Discussion

These findings suggested that CCND1, through its modulation of the tumor microenvironment, interactions with cancer-related pathways, and induction of drugs resistance, may have a significant role in the prognosis of DLBCL

References

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