



Original Article

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RPRD1B/CREPT facilitates the progression of diffuse large B-cell lymphoma by inhibiting apoptosis through the NF- κ B signaling pathwayLu Xu^{1,2,4†}, Zhi-Hao Xie^{1†}, Jun Li³, Shi Tao¹, Fang-Li Ren², Yin-Yin Wang², Zhi-Jie Chang², Xin-Bao Hao^{1,2}¹Department of Hematology, The First Affiliated Hospital of Hainan Medical University, Haikou, 570102, China²State Key Laboratory of Membrane Biology, School of Medicine, Tsinghua University, Beijing 100084, China³Heya Beijing Med-Biotech Inc., Beijing 100084, China⁴Department of Hematology, Roswell Park Comprehensive Cancer Center, NY 14263, USA

ABSTRACT

Objective: To investigate the role of RPRD1B in the progression of diffuse large B-cell lymphoma (DLBCL) and its potential as a therapeutic target.

Methods: This study analyzed RPRD1B expression in DLBCL and normal tissues using public databases and assessed its prognostic impact through survival analysis. *In vitro* and *in vivo* experiments were conducted to explore the mechanisms by which RPRD1B influences tumor growth and apoptosis.

Results: RPRD1B expression was significantly elevated in DLBCL compared to normal tissues and was associated with poor prognosis. *In vitro* and *in vivo* experiments demonstrated that RPRD1B promoted lymphoma cell proliferation and inhibited apoptosis through the NF- κ B signaling pathway.

Conclusions: RPRD1B plays a critical role in the progression of DLBCL by modulating apoptosis and cellular proliferation. Targeting RPRD1B may offer a novel therapeutic strategy for DLBCL, suggesting its potential as a prognostic marker and therapeutic target in hematological malignancies.

KEYWORDS: RPRD1B; RNAP II; Diffuse large B-cell lymphoma; NF- κ B; Apoptosis

RPRD2[2,3]. RPRD1B can bind to the phosphorylated C-terminal heptapeptide repeat domain of the POLR2A subunit of RNA polymerase II, regulate the transcriptional activity of RNAP II, and promote the transcription of target genes[4].

RPRD1B is highly expressed in most solid tumors and is associated with poor prognosis in some tumor types[1,5–17]. By regulating the transcription of tumor genes, RPRD1B can promote the proliferation, migration, and invasion of tumor cells in *in vitro* and animal experiments. However, its specific role in tumorigenesis and tumor development is still unclear[9,12,18–21].

Diffuse large B-cell lymphoma (DLBCL), the most prevalent

Significance

While the role of RPRD1B in solid tumors has been documented, its function in diffuse large B-cell lymphoma needs to be clarified. This study provides evidence that RPRD1B enhances tumor progression by inhibiting apoptosis through the NF- κ B signaling pathway, confirming its potential as a valuable target for therapeutic intervention in diffuse large B-cell lymphoma.

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1. Introduction

RPRD1B, previously identified and initially named CREPT (cell cycle-related and expression-elevated protein in tumors)[1], is a member of the RPRD protein family, which also includes RPRD1A and

subtype of non-Hodgkin lymphoma (NHL), accounts for approximately 30%–40% of adult NHL cases worldwide. Despite therapeutic advances, the prognosis for DLBCL remains variable, with a significant proportion of patients experiencing relapse or resistance to initial therapy[22,23]. The elucidation of DLBCL's molecular pathogenesis and identifying prognostic biomarkers are critical for developing targeted therapies and improving patient outcomes[24]. The expression of RPRD1B in hematological tumors and its influence on prognosis have not been reported. Moreover, the mechanisms by which RPRD1B might affect tumor cell apoptosis, especially in DLBCL, remain largely unknown. Understanding these aspects may uncover novel molecular mechanisms and offer foundational insights for innovative treatment strategies. In this study, we analyzed the expression patterns of RPRD1B in DLBCL and its association with patient prognosis.

2. Materials and methods

2.1. Data collection and analysis

The Toil unified TCGA and Genotype-Tissue Expression (GTEx) TPM RNA-seq data for RPRD1B mRNA analysis of lymphoma and normal lymphoid tissues was obtained from UCSC XENA (<https://xenabrowser.net/datapages/>). Wilcoxon rank sum test (stats package and car package) and ggplot2 package were used to visualize the data. The DLBCL sequence data of GSE 87371 and GSE 181063 (including 223 and 1310 samples respectively) were downloaded from the Gene Expression Omnibus (GEO, www.ncbi.nlm.nih.gov/geo) database, which were further used to assess the prognostic significance of RPRD1B using R package survival by integrated survival time, survival status, and gene expression data with cox model. The RPRD1B immunohistochemical staining data in normal lymph nodes and lymphoma were obtained from the Human Protein Atlas (HPA) database.

RNA-sequencing expression (level 3) profiles and corresponding clinical information for RPRD1B were downloaded from the TCGA dataset (<https://portal.gdc.cancer.gov/>). R software GSVA package was used to analyze the correlation between genes and pathway scores. The genes regulated by RPRD1B in DLBCL were analyzed using LinkedOmics (<https://www.linkedomics.org/#/>). For GO function enrichment analysis, we use the GO annotation of genes in R package org.Hs.eg.db (version 3.1.0) as background, to map genes into background set, and use R package clusterProfiler (version 3.14.3) to perform enrichment analysis for gene set enrichment. For KEGG function enrichment analysis, we used KEGG rest API (<https://www.kegg.jp/kegg/rest/keggapi.html>) to obtain the latest gene annotation of KEGG Pathway as background, to map genes into the background set, and use the R software package clusterProfiler (version 3.14.3) to perform enrichment analysis.

2.2. Patients and clinical samples

Formalin-fixed paraffin-embedded DLBCL specimens were acquired from patients who underwent immunochemotherapy at the First Affiliated Hospital of Hainan Medical University. All experimental procedures were approved by the hospital's Medical Ethics Committee (HYYFES-2021-037). Informed consent was obtained from all subjects involved in the study. The clinical information of DLBCL patients in the TCGA database is shown in Table 1.

Table 1. Clinical characteristics of DLBCL patients.

Characteristic	Low expression of RPRD1B (n=24)	High expression of RPRD1B (n=24)	P
Clinical stage, n (%)			0.97
Stage I	4 (9.5%)	4 (9.5%)	
Stage II	8 (19.0%)	4 (21.4%)	
Stage III	3 (7.1%)	2 (4.8%)	
Stage IV	5 (11.9%)	7 (16.7%)	
Treatment response, n (%)			>0.99
CR	17 (37.0%)	18 (39.1%)	
PR	2 (4.3%)	1 (2.2%)	
SD	1 (2.2%)	2 (4.3%)	
PD	3 (6.5%)	2 (4.3%)	
Sex, n (%)			0.39
Female	11 (22.9%)	15 (31.2%)	
Male	13 (27.1%)	9 (18.8%)	
Age, mean $\pm$ SD, years	55.0 $\pm$ 11.7	57.5 $\pm$ 16.1	0.55

Data was obtained from TCGA database. Treatment response was evaluated using Cheson criteria. DLBCL: diffuse large B-cell lymphoma; PD: progressive disease; SD: stable disease; PR: partial response; CR: complete response.

2.3. Cell culture and transfection

B cell lymphoma cell lines SU-DHL-2, SU-DHL-4, and SU-DHL-6 were acquired from the Shanghai Cell Bank. Cells utilized for transfection, cell cycle analysis, proliferation studies, and luciferase assays were cultured based on the methods of Lu *et al.*[1]. Certain experiments were replicated three times. Expression plasmids for human CREPT were pCMV/HACREPT and pTre2/CREPT, constructed in our lab. The plasmid pBS/U6/CREPT-si was developed using a previous protocol[1]. The target sequence for shRNA (CREPT-sh), GGACCTGAATTC ACTAGAGA, was conserved between humans and mice.

2.4. PCR and Western blot analyses

Procedures were followed as per laboratory protocols[1]. CREPT cDNA was amplified utilizing primers: forward TATAGGTACCATGTCCTCCTTCTCTGAG and reverse TATACTCGAGCTAGT CAGTTGAAAACAGGTC. Primers for Bcl-2 and cIAP1 were purchased from OriGene (Bcl-2 forward ATCGCCCTGTGGATGACTGAGT and reverse GCCAGGAGAAATCAAACAGAGGC; cIAP1

forward CAGACACATGCAGCTCGAATGAG and reverse CACCTCAAGCCACCATCACAAC). The following antibodies were used for Western blotting: RPRD1B antibody (3E10) was developed in our lab[25]. Phospho-NF- κ B p50 (Ser337) (#PA5-37658) and cIAP1 polyclonal antibodies (#PA5-29085) were both purchased from Invitrogen. From Cell Signaling Technology, Inc., we utilized β -tubulin antibody (#2146), phospho-NF- κ B p65 (Ser536) antibody (#3033S), Bcl-2 rabbit antibody (#4223S), and cleaved caspase-3 (Asp175) rabbit antibody (#9579S). All antibodies were used at a dilution of 1:1000 according to the manufacturer's instructions. Secondary antibodies from LI-COR included IRDye® 800CW Goat anti-Mouse IgG (#926-32210), IRDye® 800CW Goat anti-Rabbit IgG (#926-32211), IRDye® 680RD Goat anti-Mouse IgG (#926-68070), and IRDye® 680RD Goat anti-Rabbit IgG (#926-68071). Blots were scanned using a LI-COR Odyssey DLx Imager.

2.5. Cell proliferation and colony formation assay

The CCK-8 assay was applied to evaluate cell proliferation. Briefly, 3×10^3 cells/well were introduced into a 96-well plate. Absorbance at 450 nm was recorded using the Multiskan™ GO Microplate Spectrophotometer (ThermoFisher Scientific). Three independent experiments were conducted.

For the colony formation assay, 2×10^3 cells were allocated to a six-well plate. For colony formation in soft agar, 8000 cells were cultured in a medium containing 0.35% agar and placed in a six-well plate with 0.7% agar medium. The SU-DHL-2 and SU-DHL-6 cell lines were proliferated for 2 or 4 weeks respectively. An aggregate of 50 lymphoma cells was considered a colony and the number of colonies was enumerated.

2.6. Tumor growth *in vivo* in nude mice

The BALB/c nude mice in an SPF grade were employed to evaluate the *in vivo* effect of RPRD1B on tumor growth. All mice were provided by the Laboratory Animal Resources Center of Tsinghua University and housed in isolated and ventilated cages (maximum of six mice per cage) at the barrier facility. Animal tumor assays were conducted per a prior study[26], adhering to institutional guidelines and regulations on animal health and ethics sanctioned by the Animal Health and Ethics Committee at Tsinghua University. For the xenograft model, 5×10^6 cells were subcutaneously introduced into the right or left dorsal side of each 4-week-old male nude mouse. Three groups of mice were used, and each group comprised five mice. Tumor dimensions were recorded bi-daily for four weeks, with volume determined by the formula: Volume = (Width² × Length)/2.

2.7. Cell apoptosis assay using flow cytometry

Cells were stained using the APC Annexin V Apoptosis Detection Kit (BioLegend) according to the manufacturer's instructions and

then analyzed using flow cytometry.

2.8. NF- κ B signal analysis using luciferase reporter system

NF- κ B Luciferase Reporter, Renilla, and negative control lentivirus were purchased from BPS Bioscience (San Diego, USA). Cells were transduced with 1×10^4 TU/well NF- κ B luciferase reporter lentivirus and treated with 100 ng/mL of TNF- α according to the manufacturer's instruction.

SU-DHL-2 and SU-DHL-6 cells were briefly transfected with the specified plasmids using Lipofectamine 2000. Luciferase activity was recorded 24 hours post-transfection with the Dual-Luciferase reporter assay system (E1910, Promega, Madison, WI). Luciferase signals were normalized against Renilla luciferase activity.

2.9. Statistical analysis

Three independent replicates were performed for all cell and qPCR experiments, and five replicates were performed for animal experiments. All statistical analyses were performed in R (v3.6.3) and GraphPad Prism (version 8.0). Statistical significance was assessed using an independent sample *t*-test or the Wilcoxon rank sum test for expression data. In correlation analysis, the Pearson or the Spearman correlation coefficient was used to evaluate the correlation according to the samples' distribution. The survival R package (v3.2-8) was used for statistical survival data analysis. $P < 0.05$ was considered statistically significant.

2.10. Ethical statement

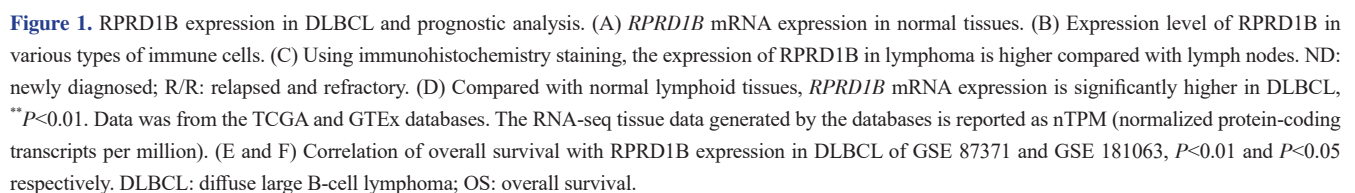
The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of the First Affiliated Hospital of Hainan Medical University (2022SRL54, Mar 24, 2022). The laboratory animal facility has been accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International and the Institutional Animal Care and Use Committee of Tsinghua University approved all animal protocols used in this study.

3. Results

3.1. Expression of RPRD1B in normal and DLBCL and prognostic analysis

RPRD1B interacts with RNA polymerase II (RNAP II), influencing its enzymatic function and regulating the transcription of a broad spectrum of genes. This protein is distributed widely across various tissues. According to mRNA sequencing data from the HPA, RPRD1B mRNA levels were particularly elevated in lymphatic tissues, the heart, skeletal muscle, and liver compared to other tissues

For prognostic analysis, we employed data from DLBCL cohorts GSE 87371 and GSE 181063, which are available in the GEO



database. After rigorous data preprocessing, we analyzed overall survival outcomes based on RPRD1B expression levels. Our stratified analysis revealed that patients with higher levels of RPRD1B expression generally had poorer prognostic outcomes, with significant differences in median survival times between groups with varying levels of RPRD1B expression, highlighting the potential of RPRD1B as a prognostic marker in DLBCL (Figure 1E and F).

3.2. RPRD1B facilitates the lymphoma cell growth *in vitro* and *in vivo*

Given the observed upregulation of RPRD1B expression in DLBCL, our study aimed to verify the role of RPRD1B in the proliferation of tumor cells. To this end, we evaluated the expression

levels of RPRD1B protein in three B-cell lymphoma cell lines and found that SU-DHL-2 cells exhibited significantly higher levels of RPRD1B compared to those found in normal lymph node tissue, and the RPRD1B expression in SU-DHL-6 was only slightly increased (Figure 2A and B). To investigate the functional role of RPRD1B in promoting cell growth, we genetically modified the SU-DHL-6 cell line to overexpress RPRD1B through a lentiviral vector. We employed RNA interference to reduce RPRD1B expression in the SU-DHL-2 cell line. These manipulations allowed us to directly assess the impact of RPRD1B levels on cell proliferation (Figure 2C and D).

Our experiments revealed that the overexpression of RPRD1B in SU-DHL-6 cells led to a significant increase in their proliferation rate *in vitro* (Figure 2F). Conversely, diminishing RPRD1B expression in

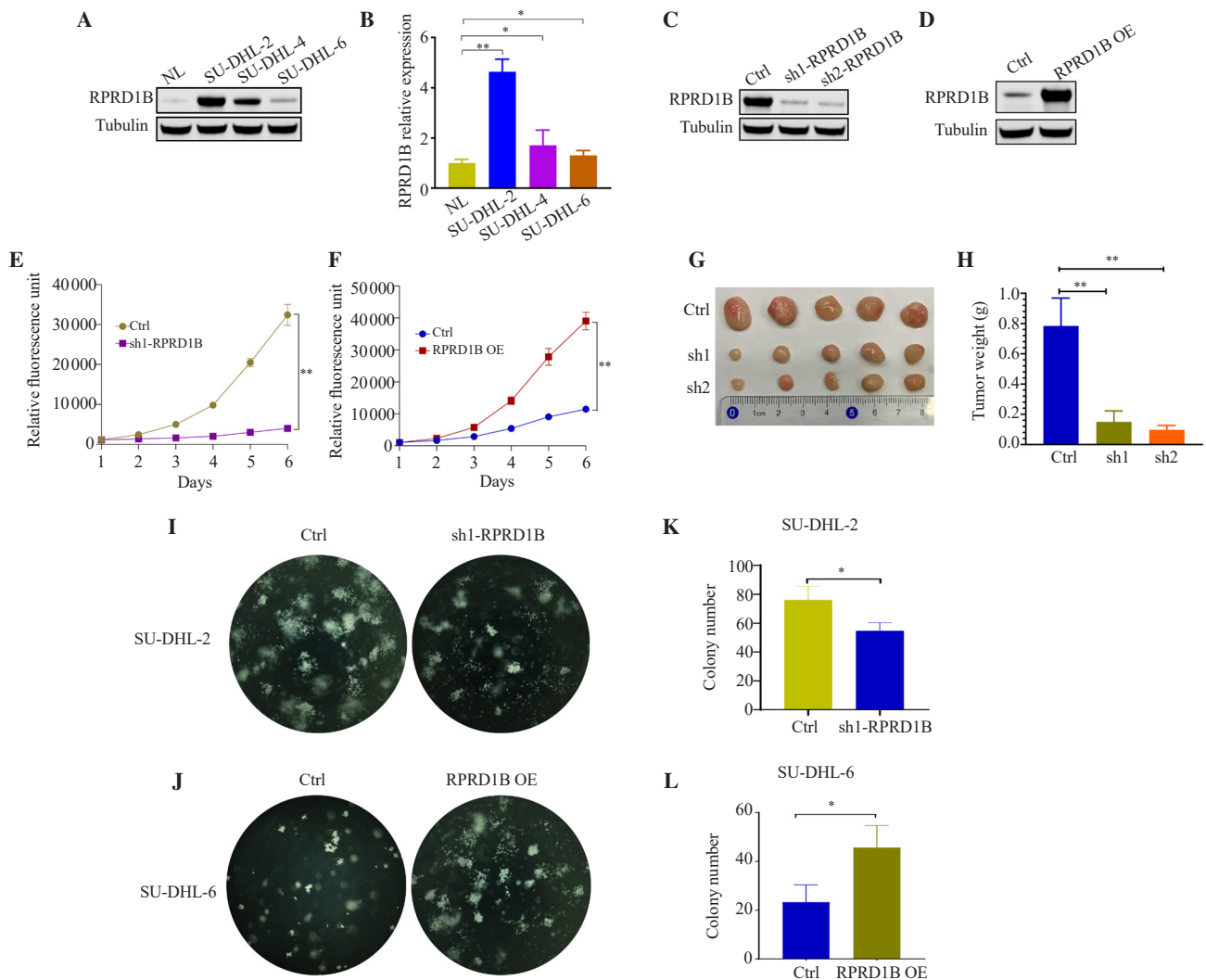
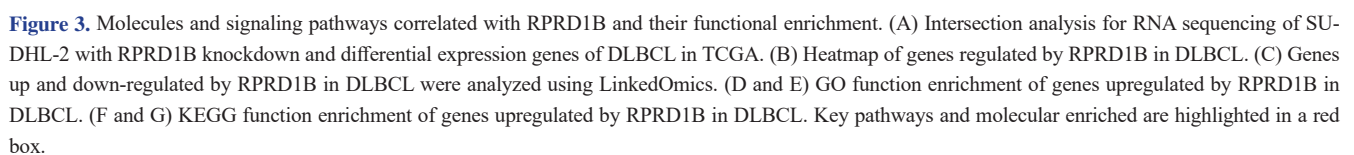


Figure 2. RPRD1B expression promotes lymphoma cell proliferation and tumor growth in mice. (A and B) RPRD1B protein expression in lymphoma cell lines. Western blot was performed using normal lymph node (NL), and three other B cell lymphoma cell lines. (C) RPRD1B was knocked down in SU-DHL-2 (sh1, sh2) using a shRNA vector. (D) RPRD1B was overexpressed in SU-DHL-6 (OE) using an expression vector. (E) Knockdown of RPRD1B inhibits SU-DHL-2 cell proliferation. (F) Overexpression of RPRD1B promotes SU-DHL-6 cell growth. (G and H) RPRD1B knockdown inhibits lymphoma growth in nude mice. (I and K) Knockdown of RPRD1B inhibits the colony formation of lymphoma cells in soft agar. (J and L) RPRD1B overexpression facilitates the colony formation of lymphoma cells in soft agar. * $P < 0.05$, ** $P < 0.01$.



SU-DHL-2 cells resulted in a notable decrease in their growth rate (Figure 2E) and a substantial reduction in their clonogenic capacity, an important marker of malignancy of tumor cells (Figure 2I and K).

To corroborate these findings using an animal model, when SU-DHL-2 cells with decreased RPRD1B expression were implanted into nude mice, their capacity to form tumors *in vivo* was significantly diminished (Figure 2G and H).

3.3. GO/KEGG analysis of regulated genes by RPRD1B in DLBCL

By leveraging the LinkedOmics platform, our study has identified 192 genes that exhibit a strong correlation with RPRD1B expression in the context of DLBCL, using data derived from both The Cancer Genome Atlas (TCGA) DLBCL differential expression dataset and our laboratory's mRNA sequencing analysis. This intersection analysis, adhering to strict statistical thresholds ($P < 0.05$, $FDR < 0.5$), highlighted 148 genes as being significantly upregulated and 44 as downregulated in relation to RPRD1B expression (Figure 3A and C). The clustering heatmap presented in our results visualizes the expression levels of RPRD1B among these genes (Figure 3B).

For the genes significantly correlated with RPRD1B (148 upregulated and 44 downregulated), we carried out GO and KEGG enrichment analyses. The analyses revealed that the upregulated genes predominantly fall within categories related to cellular nuclear proteins, cytoskeletal components, and pathways crucial to cancer

biology, such as NF- κ B signaling and apoptosis (Figure 3D and F). Among these regulated entities, BIRC2 (also known as cIAP1) and its associated molecular network were pinpointed for their critical involvement in the NF- κ B pathway and apoptosis mechanisms in lymphoma (Figure 3G).

Building on these insights from gene functional enrichment, we scrutinized the association between RPRD1B and pivotal pathways using their gene expression signatures. This exploration uncovered significant positive correlations between RPRD1B expression and those most critical signaling pathways, including NF- κ B, PI3K-AKT, cell proliferation, and the cell cycle G₂M checkpoint, all of which are integral to the pathogenesis, progression, and therapeutic responsiveness of lymphoma (Figure 4A-D). Exploring the connection between RPRD1B and crucial elements of the NF- κ B and apoptosis pathways, we found that RPRD1B showed significant positive associations with NFKB1, RELA (part of the NF- κ B complex), BIRC2 (also known as cIAP1), and Bcl-2 (Figure 4E-H). These relationships suggest that RPRD1B plays a significant role in the processes that control cell survival and death.

3.4. RPRD1B inhibits the tumor cell apoptosis via regulating the NF- κ B pathway

In this study, we discovered that lymphoma cell lines exhibiting high levels of RPRD1B expression experienced increased proliferation both *in vitro* and *in vivo*. Conversely, reducing RPRD1B

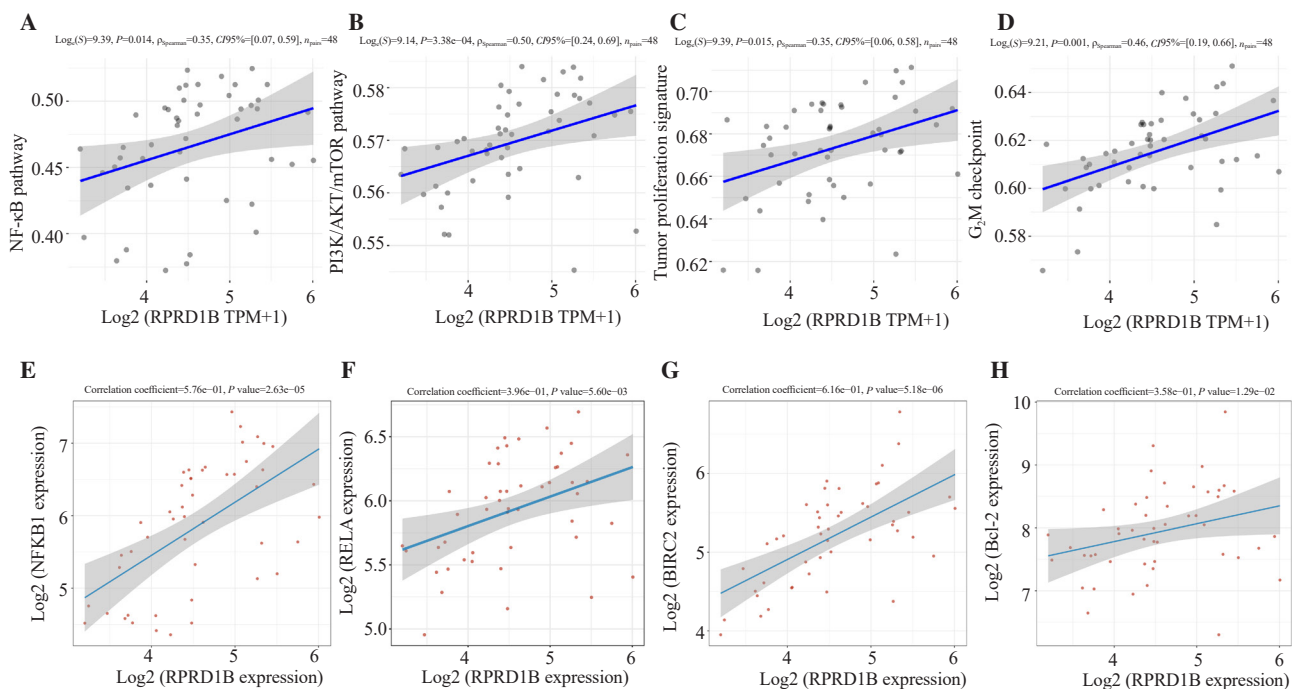


Figure 4. Correlation analysis of RPRD1B with signaling pathway and tumor gene expression. (A-D) Signaling pathways are significantly associated with RPRD1B in DLBCL. (E-H) Correlation analysis between key molecules in NF- κ B and apoptosis and RPRD1B expression in DLBCL.

expression led to a significant decrease in cell proliferation. To understand how increased RPRD1B expression contributes to the enhanced growth capabilities of lymphoma cells, we investigated its impact on cell apoptosis, a form of programmed cell death.

Our findings revealed that, compared to control cells, apoptosis rates were higher in SU-DHL-2 lymphoma cells with reduced RPRD1B expression, increasing from 6.63% to 19.96% (Figure 5A and B). This increase in apoptosis was partially mitigated when cells were stimulated with TNF- α , a protein that can influence cell survival and death (Figure 5C and D). Additionally, quantitative PCR analyses showed that diminishing *RPRD1B* expression led to decreased levels of anti-apoptotic genes *Bcl-2* and *cIAP1* (Figure 5E). Western blot analyses corroborated these results, showing reduced protein levels of Bcl-2 and cIAP1 and increased levels of cleaved caspase 3, a marker of apoptosis, upon RPRD1B

knockdown (Figure 5H). These results suggest that RPRD1B plays a critical role in regulating cell apoptosis in lymphoma cells, with its high expression associated with decreased apoptosis, which could contribute to tumor progression.

Further investigations into the molecular mechanisms behind this regulation revealed a significant association between RPRD1B expression and the NF- κ B signaling pathway, which is known to control the expression of anti-apoptotic proteins such as Bcl-2, Bcl-xL, XIAP, and cIAP1. Nuclear factors NF- κ B1 and RELA strongly correlated with RPRD1B expression, suggesting a co-regulatory role in the transcription of target genes involved in cell survival and apoptosis. Using an NF- κ B luciferase reporter system, we demonstrated that knocking down RPRD1B expression significantly inhibited NF- κ B transcriptional activity in lymphoma cells (Figure 5F), while overexpression of RPRD1B enhanced it (Figure 5G).

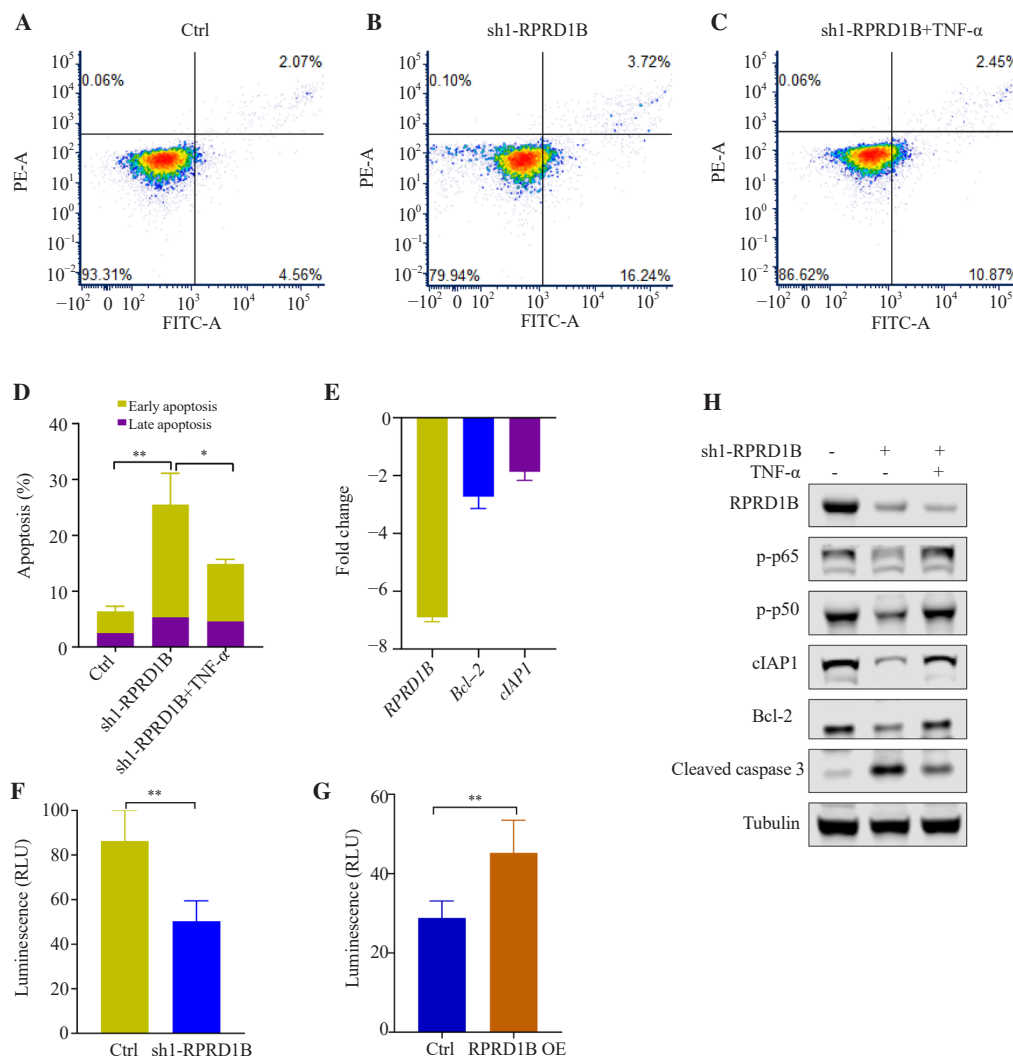


Figure 5. RPRD1B inhibits the DLBCL apoptosis via regulating the NF- κ B. (A-D) Knocking down the RPRD1B in SU-DHL-2 results in cell apoptosis, partially reversed by adding TNF- α . (E) Knocking down the RPRD1B causes less expression of Bcl-2 and cIAP1. (F) NF- κ B signaling is inhibited by knocking down the RPRD1B using a luciferase reporter system. (G) NF- κ B signaling is stimulated by overexpressing the RPRD1B. (H) Western blot results show that RPRD1B regulates the NF- κ B and apoptosis molecules. * $P < 0.05$, ** $P < 0.01$.

Additionally, the phosphorylation of NF- κ B subunits p50 and p65 was decreased by RPRD1B knockdown and partially restored by TNF- α addition (Figure 5H).

4. Discussion

The RPRD1B protein interacts with RNA polymerase II (RNAP II) by forming both homodimers and heterodimers with RPRD1A. This interaction plays a vital role in regulating gene expression[3,4]. Through its role in transcriptional regulation, RPRD1B has been demonstrated to affect the transcription and expression of genes associated with tumor growth and metastasis, including CCND1, CCNB1, CCNE, CDK1, CDK4, CDK6, and c-MYC[27,28]. This regulatory function contributes to the malignant transformation of cells that supports tumor progression and may increase tumor cell resistance to radiation and chemotherapy treatments[29–31]. However, the specific role of RPRD1B in the development of hematological malignancies, particularly lymphomas, remains to be fully elucidated.

Utilizing public databases, this study reviewed RPRD1B distribution as a nuclear protein in both normal blood cells and DLBCL tumors. Given the high RPRD1B expression in hematopoietic tissues and the limited understanding of its role in blood cancers, we analyzed two DLBCL cohort datasets to investigate the impact of RPRD1B expression on patient prognosis. Our analysis indicated a significant increase in RPRD1B expression in DLBCL tissues compared to normal tissues, with high RPRD1B levels correlating with poorer patient outcomes. To further investigate RPRD1B's role in promoting lymphoma cell growth, we manipulated its expression in the SU-DHL-2 and SU-DHL-6 cell lines, observing that decreased RPRD1B expression resulted in reduced cell proliferation, whereas increased RPRD1B expression enhanced cell growth. This relationship was also confirmed in a mouse xenograft model, where reduced RPRD1B expression in transplanted SU-DHL-2 cells led to diminished tumor growth *in vivo*.

Exploring the underlying mechanisms, we sequenced RNA samples from DLBCL cell lines and compared differentially expressed genes with the LinkedOmics database, identifying 192 genes significantly regulated by RPRD1B. Our analysis revealed positive correlations between RPRD1B and pathways critical for lymphoma development, including PI3K/AKT/mTOR, the G₂M checkpoint, and the NF- κ B signaling pathway, along with anti-apoptotic proteins Bcl-2 and cIAP1. Further experimental studies underscored RPRD1B's ability to foster lymphoma cell proliferation by dampening apoptosis, primarily through the modulation of the NF- κ B signaling pathway.

The interaction between NF- κ B and apoptotic pathways in lymphoma is complex and bidirectional. NF- κ B can inhibit apoptosis by inducing the expression of anti-apoptotic genes such as Bcl-2,

Bcl-xL, and cIAPs[32,33]. These proteins counteract the pro-apoptotic signals, thus providing a survival advantage to lymphoma cells[34]. Additionally, NF- κ B regulates the expression of various cytokines and growth factors that can promote lymphoma cell survival and proliferation[35,36]. The dysregulation of NF- κ B and apoptosis contributes to the pathogenesis and progression of lymphoma and resistance to chemotherapy. Many chemotherapeutic agents exert their effects by inducing apoptosis in cancer cells. Therefore, the overexpression of NF- κ B-mediated anti-apoptotic genes can render lymphoma cells resistant to these treatments[37,38]. Studies have shown that downregulation of apoptosis inhibiting proteins can reverse cell drug resistance[39], and combination with kinase-targeting drugs may lead to better therapeutic outcomes[40,41].

The study provides new insights into the role of RPRD1B in the progression of DLBCL and its potential as a therapeutic target. However, several limitations must be acknowledged to accurately contextualize these findings. A primary limitation is our reliance on cell line models and data from public databases, which may not capture the full spectrum of heterogeneity and microenvironmental interactions characteristic of DLBCL in clinical scenarios. Future research should therefore include patient-derived xenograft models and more diverse DLBCL subtypes to better reflect the disease's biological and clinical complexities.

Furthermore, while the conclusions drawn from retrospective data analysis suggest a strong association between high RPRD1B expression and poor prognostic outcomes, these findings are correlational and do not establish causality. Prospective studies are necessary to confirm these associations and to assess the therapeutic efficacy of targeting RPRD1B in clinical research.

In conclusion, this study suggests that RPRD1B may enhance the progression of DLBCL by promoting cell proliferation and reducing apoptosis through the NF- κ B pathway. While these findings highlight the potential of RPRD1B as a therapeutic target, they are based on cell line models and retrospective data analysis. Consequently, further research involving clinical trials and patient-derived models is necessary to confirm these results and fully ascertain the therapeutic value of targeting RPRD1B in DLBCL.

Conflict of interest statement

The authors declare no conflict of interest.

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Data availability statement

The data supporting the findings of this study are available from the corresponding authors upon request.

Authors' contributions

LX designed the work, performed the experiments and wrote the original draft. ZHX conducted experiments and collected data. JL, ST and FLR established the experimental methods and conducted the experiments. YYW and ZJC supervised the project. XBH analyzed and interpreted the data and revised the manuscript. All authors have read and approved the final manuscript.

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