

Differential expression analysis of key cellular helicases in EBV-positive and EBV-negative prostate cancer tissues

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Abstract

Introduction:

Dysregulation of helicase proteins, key cellular proteins involved in DNA replication, has been shown to promote genomic instability and cancer development by affecting DNA repair, genome maintenance, and epigenetic regulation of tumor suppressors and oncogenes in malignant cells. A limited number of studies have reported that EBV-positive tissues exhibit increased expression of oncogenes; however, the link between EBV and changes in helicase expression and their effects on prostate cancer (PCa) has not been explored. Therefore, we aimed to analyze the expression of key prostate-associated helicases using the TCGA PCa dataset, examine their expression in EBV-positive and -negative PCa tissues, and correlate helicase expression with Gleason scores, a marker of PCa aggressiveness.

Materials and methods

PCa transcriptome data (TCGA-PRAD) was analyzed to examine differential expression of key helicase genes in PCa versus normal samples using the DESeq2 package. In the second phase, differential expression analysis of helicase genes was examined in EBV-positive and -negative PCa tissue samples, using an in-house qPCR array. Finally, a two-stage nested ordinal logistic regression was conducted to assess the impact of helicase expression (additive model) and together with EBV status (interaction model) on Gleason scores.

Results

Differential gene expression analysis of the TCGA-PRAD dataset showed significantly different expression ($p_{\text{adj}} < 0.05$) of several helicase genes, including *BLM*, *RAD54L*, and *CACHD1*, between PCa and normal samples. Helicase gene expression analysis, using qPCR, in EBV-positive versus EBV-negative PCa samples showed that helicase genes, namely *CHD4*, *DHX15*, *ERCC2*, *RAD54B*, *DDX46*, and *RAD54L*, exhibit greater than 2-fold differences in expression. Comparative analyses of TCGA-PRAD and qPCR-based gene expression data showed a concordant expression pattern across nine genes. Seven genes, i.e., *RAD54L*, *ERCC2*, *DHX15*, *SRCAP*, *RECQL5*, *YTHDF2*, and *RAD54B*, were upregulated in both datasets, whereas *SMARCA5* and *CACHD1* were downregulated in both. Initial statistical assessment via additive modeling showed significant associations ($p < 0.05$) between high expression of helicases, including *CHD4*, *RAD54B*, *DDX46*, and *RAD54L*, and Gleason scores (all $p < 0.05$). Interaction analysis revealed that only *CHD4* showed a significant EBV-dependent association with Gleason scores and helicase expression (Type III Wald $\chi^2(1) = 18.675$, $p < .001$). While *RAD54B* showed a significant additive effect ($\chi^2(6) = 4.481$, $p = 0.034$), its interaction with EBV status was only marginally significant (Type III Wald $\chi^2(1) = 3.771$, $p = 0.052$).

Conclusion

This study shows that EBV presence in PCa tissues significantly alters the expression of key helicase genes, including *CHD4*, *DHX15*, *ERCC2*, *RAD54B*, *DDX46*, and *RAD54L*, which are linked to genomic instability and may relate to PCa progression and aggressiveness. Furthermore, expression of the helicases CHD4 and RAD54B correlated with higher Gleason scores, with EBV presence serving as a moderating factor. These findings suggest that the interaction between EBV and dysregulated helicases may drive PCa progression, improving our understanding of EBV-associated prostate oncogenesis.

INTRODUCTION

Certain viruses, such as Human Papillomavirus (HPV) and Epstein-Barr virus (EBV), have been associated with prostate cancer (PCa); however, the role of these viruses in prostate tumorigenesis is poorly understood^{1,2}. A meta-analysis based on 927 PCa samples showed a 33% pooled prevalence of EBV in PCa tissues and increased odds (OR = 2.38, $p = 0.002$) of higher Gleason scores and EBV presence in PCa tissues³. Previous studies from our group have reported that EBV-positive tissues exhibited higher expression of drivers of EMT genes, as well as higher expression of PCa-associated OncomiRs linked to PCa aggressiveness⁴. Beyond this, the role of other genes and pathways involved in EBV-associated prostate carcinogenesis has not been explored.

Helicases are key cellular enzymes that catalyse the unwinding of complementary strands of DNA or RNA in an ATP-dependent fashion, and remodel nucleic acids or nucleic acid proteins⁵. Dysregulated activity of several DNA and RNA helicases, such as RecQL4, DEAD box RNA helicase p68 (Ddx5), and DHX9, has been implicated in PCa oncogenesis⁶. DEAD box RNA helicase p68 (Ddx5) has a regulatory role and has been identified as a novel androgen receptor transcriptional co-activator, which is overexpressed in PCa^{7,8}, while *DHX9* on chromosome 1q25 has been mapped to the major susceptibility locus associated with PCa^{8,9}.

EBV latency-associated proteins, such as LMP1, EBNA1, and EBNA3C, have been shown to enhance genomic instability and cause histone H2AX to phosphorylate and induce DNA breaks^{10,11}. Additionally, EBV protein SM (BMLF1) has been shown to bind DHX9 helicase to suppress its antiviral activity, thereby facilitating the production of infectious viral particles¹². However, the link between EBV presence in PCa, changes in helicase expression, and its effect on PCa oncogenesis remains unexplored.

In this study, we analysed the expression of key prostate-associated helicases using the TCGA dataset, then compared their levels in EBV-positive and EBV-negative PCA tissues, and finally examined the correlation between helicase expression and higher Gleason scores, a marker of PCa aggressiveness¹³.

MATERIALS AND METHODS

Retrieval of prostate cancer transcriptomics data and analysis of differential expression of helicases in prostate cancers

TCGA-PRAD transcriptomics data, i.e., the raw read counts generated by the STAR alignment pipeline, from PCa (n = 497) and normal samples (n = 52) were retrieved from the Genomic Data Commons (GDC) portal using the *TCGAbiolinks* package in R^{14,15}. The data were processed to remove duplicates and differential gene expression analysis was performed comparing PCa versus normal samples using the *DESeq2* package. Next, transcripts with low counts were filtered to only keep genes with ≥ 10 counts in at least 15 samples. The p-values from the Wald test were used to generate adjusted p-values using the Benjamini-Hochberg false discovery rate (FDR). For this study, only the following DNA, RNA, and chromatin-remodeling helicase genes: *ERCC2*, *DHX9*, *INTS6*, *SKIC2*, *YTHDF2*, *DDX17*, *CACHD1*, *CHD2*, *CHD3*, *CHD4*, *CHD5*, *ERCC3*, *RAD54L*, *SMARCA5*, *SRCAP*, *BLM*, *RECQL5*, *DHX15*, *CHD6*, *RAD54B*, and *DDX46*, which have been reported to play major roles as regulators of various cellular processes, such as transcriptional regulation, genome stability, chromatin remodeling, DNA repair, and RNA splicing/metabolism, and are frequently dysregulated in PCa^{6,16–19} were used. In our analysis, differentially expressed helicase genes with adjusted p < 0.05 and log2 fold change > 0.5 or < -0.5 were considered significantly up- and down-regulated genes. The *ggplot2* and *ggrepel* packages were used in R to generate volcano plots and divergent bar plots.

Histopathological analysis of EBV-positive and -negative PCa tissue samples

Ninety-nine PCa tissues, which were previously characterized as EBV-positive (n = 39) and EBV-negative (n = 60)⁴ were initially screened for quantity, quality, and tumor content. All assessed samples were identified as prostate adenocarcinoma of the acinar subtype²⁰. Based on this, 12 EBV-positive and 12 EBV-negative (1:1 ratio) PCa tissues with adequate tissue quantity, quality, and tumor content were selected.

The previous histopathological analysis of tissues showed that EBV-positive PCa samples had statistically significantly higher tumor grades (Gleason scores) and a higher frequency of perineural invasion, when compared with EBV-negative PCa samples⁴. To reconfirm that the selected tissues were comparable in histopathologic features, hematoxylin and eosin staining was used, and tissues underwent histopathologic characterization using the WHO 2016 prostate cancer grade group system (ISUP-2014)^{21,22}. The Gleason scores in both EBV-positive and EBV-negative PCa tumor samples were subsequently analyzed.

RNA extraction, cDNA conversion, and differential expression analysis of helicase genes in EBV-positive and EBV-negative PCa tissues using qPCR

RNA was extracted from the shortlisted PCa tissues using the TRIzol-chloroform method. Briefly, samples were treated with 200 μ l chloroform and 700 μ l TRIzol, then centrifuged for phase separation.

RNA was precipitated from the aqueous phase using 1000 µl of chilled isopropanol²⁰. Pellets were washed with 70% ethanol, air-dried, resuspended in 50 µl of nuclease-free water, and stored at – 80°C.

Prior to cDNA synthesis, total RNA was treated with DNase I to eliminate any residual genomic DNA. In a 0.2 ml tube, 1 µg of total RNA was mixed with 1 µl of 10X reaction buffer (containing MgCl₂), 1 µl of RNase-free DNase-I (1 U/µl; Thermo Fisher Scientific, Cat. No. EN0521), and nuclease-free water to bring the total volume to 10 µl. This mixture was incubated for 30 min at 37°C using an Eppendorf Master cycler X50a (Germany). Afterward, 1 µl of 50 mM EDTA was added to inactivate the DNase-I and protect the RNA from degradation, followed by a 10-min incubation at 65°C²⁰. The resulting DNase-treated RNA was then reverse-transcribed into cDNA using the OneScript plus cDNA synthesis kit (ABM, Canada; Cat. No. G236), according to the manufacturer's protocol, and the cDNA was stored at – 20°C until needed.

The following helicases or helicase-associated genes, namely *ERCC2*, *DHX9*, *INTS6*, *SKIC2*, *YTHDF2*, *DDX17*, *CACHD1*, *CHD2*, *CHD3*, *CHD4*, *CHD5*, *ERCC3*, *RAD54L*, *SMARCA5*, *SRCAP*, *BLM*, *RECQL5*, *DHX15*, *CHD6*, *RAD54B*, and *DDX46*, were selected based on their reported differential expression and roles in PCa^{6,16}. 2µl of cDNA sample was combined with a mixture containing 4 µl of BlasTaq™ (2X) qPCR master mix (ABM, Canada, Cat. No. G891), forward and reverse gene-specific helicase primers (Table 1), and nuclease-free water to a final reaction volume of up to 10µl in 0.2 ml tubes (Bio-Rad Laboratories, USA, Cat. No. TLS0851). The prepared reactions were subjected to the following thermal cycling conditions in a Bio-Rad 1000 CFX96 thermal cycler (Bio-Rad Laboratories, USA): Initial denaturation for 10 minutes at 95°C, followed by 40 cycles of denaturation for 15 seconds at 95°C and primer annealing at 60–65°C for 1 minute for all genes. A melt curve analysis was performed between 55°C and 95°C, with an increment of 0.5°C every 5 seconds, to assess specificity of the product. The expression of each gene was calculated using the ΔCT method, while fold-change was calculated using the $2^{-\Delta\Delta CT}$ method²³. For normalization, β -actin was used as the housekeeping gene for all other genes. A two-fold difference in the expression of helicase genes between EBV-positive and -negative tissues was considered significant.

Next, helicase expression between TCGA and qPCR data from EBV-positive and EBV-negative PCa tissues was compared. The analysis particularly emphasized the direction (up- or downregulation) of helicase gene expression. For this analysis, log₂FC data were converted to FC using the formula, $FC = 2^{\log_2 FC}$ for positive values, and $FC = -1/2^{\log_2 FC}$ for negative values, to ensure comparisons are on the same scale.

Association between helicase expression, EBV status, and high Gleason scores

To examine relationships between helicase expression, EBV status, and PCa severity (indicated by high Gleason scores), an ordinal logistic regression was performed in two stages. First, an additive model evaluated the main effects of helicase expression (cycle threshold values) and Gleason scores. The proportional odds assumption was assessed via the Test of Parallel Lines; a significant Chi-square result

indicates that the relationship between predictors and the outcome varies across Gleason score thresholds. Based on the additive model results, an interaction model (EBV*Helicase) was implemented, and the significance of these effects was tested using the Type III Wald Chi-Square test. All statistical analyses were conducted with IBM SPSS Statistics (version 22.0), with significance set at $p < 0.05$.

RESULTS

Differential helicase gene expression based on the TCGA PCa dataset

Analysis of TCGA-PRAD data showed significantly increased expression of several helicases, especially *BLM* (Log2FC = 0.734) and *RAD54L* (Log2FC = 0.920), while decreased expression of *CACHD1* (Log2FC = -1.345) and *CHD5* (Log2FC = -1.207) in PCa tissues compared to normal samples (Fig. 1).

Histopathological and helicase gene expression analysis in EBV-positive and -negative PCa tissues and comparison between qPCR (differentially expressed in EBV-positive PCa tissues) and TCGA data

Based on histopathological analysis, tissues from both EBV-positive and EBV-negative groups had comparable tumor grades and Gleason scores, ranging from prognostic grade group 1 (Gleason scores 6/10) to prognostic grade group 5 (Gleason scores 10/10)²¹. The EBV-positive PCa tissues had a mean total Gleason score of 7.67, whereas EBV-negative PCa tissues had a mean total Gleason score of 8.33 (Fig. 1).

The gene expression analysis, using qPCR, showed *DHX15* (FC = 4.52), *ERCC2* (FC = 2.59), *RAD54B* (FC = 2.88), *DDX46* (FC = 2.07), and *RAD54L* (FC = 2.13) to exhibit significantly increased expression, while only *CHD4* had significantly decreased expression (FC=-2.29) in EBV-positive PCa samples compared to EBV-negative PCa samples (Fig. 3).

Comparative analyses of qPCR (FC) and TCGA (Log2FC converted to FC) data (Fig. 4), based on directionality of expression, showed high consistency in the expression of nine helicase genes (Fig. 4). Specifically, seven genes, namely *RAD54L* (TCGA-FC: 1.89; qPCR-FC: 2.19), *ERCC2* (TCGA-FC: 1.25; qPCR-FC: 2.59), *SRCAP* (TCGA-FC: 1.14; qPCR-FC: 1.23), *DHX15* (TCGA-FC: 1.14; qPCR-FC: 4.52), *RECQL5* (TCGA-FC: 1.13; qPCR-FC: 1.01), *YTHDF2* (TCGA-FC: 1.10; qPCR-FC: 1.37) and *RAD54B* (TCGA-FC: 1.01; qPCR-FC: 2.88) demonstrated consistently increased expression across TCGA and qPCR data, whereas two genes, *SMARCA5* (TCGA-FC: -1.14; qPCR-FC: -1.14) and *CACHD1* (TCGA-FC: -2.54; qPCR FC: -1.09), showed consistently decreased expression across TCGA and qPCR data (Supplementary Table 1).

Association of helicase expression and EBV status with high Gleason scores

To examine relationships between helicase expression, EBV status, and PCa severity (defined in this study by high Gleason scores), two nested ordinal logistic regression models were used. The additive model revealed that several helicases, including *CHD4*, *RAD54B*, *DDX46*, and *RAD54L*, were significantly associated with Gleason scores (all $p < 0.05$; Table 1). Further analysis using an interaction model (EBV*Helicase) revealed a highly significant interaction effect only between EBV status and *CHD4* expression on Gleason Scores (Type III Wald $\chi^2 (1) = 18.675$, $p < .001$). In contrast, while *RAD54B* showed a significant additive effect ($\chi^2 (6) = 15.846$, $p = 0.015$), its interaction with EBV status was only marginally significant ((Type III Wald $\chi^2 (1) = 3.771$, $p = 0.052$).

Table 1

Statistical analysis of the association between Helicase expression, EBV status, and Gleason Score. The additive model evaluated the association between helicase expression and Gleason's score, while the interaction model (EBV status * CT values) assessed the association between helicase expression and Gleason's score with EBV status as an interaction term (mediator). Bold text indicates statistically significant findings ($p < 0.05$).

Helicases	Additive Model		Interaction Model		
	Chi-Square ($Df = 6$)	p-value	Source	Wald Chi-Square ($Df = 1$)	p-value
<i>CHD4</i>	31.519	0.000	EBV status	19.089	0.000
			CT values	1.366	0.242
			EBV status * CT values	18.675	0.000
<i>DHX15</i>	5.391	0.495	EBV status	2.964	0.085
			CT values	6.906	0.009
			EBV status * CT values	2.794	0.095
<i>ERCC2</i>	9.162`	0.165	EBV status	2.508	0.113
			CT values	1.085	0.098
			EBV status * CT values	2.241	0.134
<i>RAD54B</i>	15.836	0.015	EBV status	4.481	0.034
			CT values	1.178	0.278
			EBV status * CT values	3.771	0.052
<i>DDX46</i>	14.534	0.024	EBV status	2.112	0.146
			CT values	0.903	0.342
			EBV status * CT values	1.624	0.202
<i>RAD54L</i>	19.784	.003	EBV status	0.529	0.467
			CT values	0.164	0.686
			EBV status * CT values	0.309	0.578

DISCUSSION

The dysregulation of DNA and RNA helicases is known as a major driver of PCa progression, as these enzymes play a pivotal role in genome maintenance, transcription, and chromatin remodeling in the cell^{24,25}. EBV is increasingly recognized as a significant factor in PCa pathogenesis and progression, as EBV-positive PCa tissues have been reported to show more aggressive histopathological features, such as

higher mean Gleason scores and higher frequency of perineural invasion cases as compared with EBV-negative PCa tissues^{4,20}. Furthermore, EBV-positive tumors have distinct molecular signatures, such as increased vimentin expression and altered expression of several oncomiRs. A recent meta-analysis found that EBV presence was associated with a significant increase in the odds of having moderate-to-high Gleason scores (OR = 2.38, p = 0.002)³. However, the relationship between EBV infection, helicase expression, and PCa has not been explored. EBV infection in PCa is known to dysregulate the host cell cycle and DNA repair machinery, as evidenced by the concurrent modulation of genes such as CHEK2 and CDC20⁴.

EBV-associated carcinogenesis depends on dysregulation of cellular chromatin and RNA machinery for it to both maintain latent EBV infection and remain in an immune-evasive episomal state, and upon periodic reactivations often co-opt host repair systems²⁶. *CHD4*, a nucleosome remodeler, has been reported to be direct epigenetic repressor of EBV lytic reactivation, thereby potentially contributing towards maintenance of latent EBV infection²⁷. The increased expression of *RAD54B* DNA helicase in EBV-positive PCa tissues, observed in our study, may indicate the cell's attempt to repair potentially aberrant DNA damage response driven by EBV infection²⁸. This enhanced DNA repair capacity may prevent apoptosis in EBV-infected prostate epithelial cells, thereby allowing them to survive and accumulate the subsequent genetic mutations required for carcinogenesis²⁹. Similarly, the significantly increased expression of *DDX46*, a DEAD-box RNA helicase, in EBV-positive PCa tissues points toward the viral manipulation of host RNA splicing and may relate to enhanced genomic instability and accumulation of mutations³⁰. Previous studies have shown dysregulated expression of *DDX46* in esophageal squamous cell cancer³¹. The significantly decreased expression of *CHD4* in EBV-positive PCa tissues as compared to EBV-negative PCa tissues, as observed in our study, also has implications in PCa oncogenesis. *CHD4* plays a significant role in androgen signaling, and its corresponding association with castration-resistant prostate cancer has also been reported^{32,33}, therefore, suggesting that *CHD4* might be involved in the EBV-associated PCa progression and severity, which may further be explored in future studies. *RAD54L* is involved in homologous recombination repair, and it has been reported to be suppressed by enzalutamide, the AR pathway inhibitor, in castration-resistant prostate cancer cells³⁴ and it remains one of assessed gene to assess PARP inhibitor sensitivity in advanced prostate cancers³⁵

Comparative analyses of TCGA-PRAD and qPCR data, based on directionality of expression, showed consistently increased expression of *RAD54L*, *ERCC2*, *DHX15*, *SRCAP*, *RECQL5*, *YTHDF2*, and *RAD54B*, while *SMARCA5* and *CACHD1* showed decreased expression in PCa samples compared to normal, and EBV-positive PCa tissues compared to EBV-negative tissues, respectively. Broadly, the upregulated genes are involved in genome maintenance and post-transcriptional regulation, whereas the downregulated genes are associated with DNA repair and chromatin remodeling. For example, *RECQL5* has been shown to be involved in various functions involving DNA integrity and chromatin integrity³⁶, whereas *YTHDF2* and *DHX15* are important for RNA fate and have a role in the antiviral arm of the immune system^{37,38}.

Since RECQL5 is crucial for cell proliferation and genomic stability, assisting cancer cells in coping with the accumulation of endogenous DNA damage and oxidative stress encountered during rapid division, the higher gene expression of DNA repair and RecQ Helicase (RECQL5) may indicate increased DNA damage response in PCa, particularly EBV-positive PCa samples ^{16,39}.

YTHDF2 is reported to be upregulated in PCa and has been shown to be associated to overall poor survival ⁴⁰. The increased expression of DEAD/H-box RNA helicases, including DHX15, highlights their critical role in modulating androgen receptor signaling; for instance, DHX15 can act as a potent androgen receptor co-activator, and its upregulation may be correlated with higher Gleason scores ^{41,42}. The differential expression of chromatin remodeling helicases, including the downregulation of *SMARCA5*, may be related to epigenetic reprogramming; especially the concurrent downregulation of *SMARCA5* suggests the loss of specific chromatin-remodeling tumor-suppressive functions and may be associated with PCa progression ^{43,44}. *SMARCA5* has been shown to act as an oncogene and has been found to be associated with progression of PCa ^{45,46}. It remains a functional connection between the androgen pathway and chromatin remodeling, and the *SMARCA5*-*USP3* axis has been proposed to be a candidate therapeutic target in chemo-resistant PCa ⁴⁷.

The incorporation of ordinal logistic regression models in our study provides a nuanced understanding of how helicase dysregulation might contribute to PCa severity. Our analysis highlights two distinct mechanisms of PCa severity: one an EBV-independent influence of DNA repair and RNA splicing helicases (*RAD54B*, *RAD54L*, and *DDX46*), and a targeted, EBV-dependent effect involving *CHD4* and potentially *RAD54B* ^{48,49}.

In conclusion, our findings indicate that the potential dysregulation of DNA, RNA, and chromatin-remodeling helicases might be associated with PCa through processes involving genomic instability under replication stress and potential orchestration of epigenetic rewiring. Analysis of the helicases' gene expression profiles with the EBV viral status has revealed distinct potential molecular vulnerabilities that can be further investigated to understand the potential role of EBV-mediated helicase-driven progression of PCa and can also potentially identify dysregulated helicases as targets for drug therapy.

Declarations

Informed Consent

Statement: Informed consent was obtained from all subjects involved in the study.

Conflicts of Interest:

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to

publish the results.

Author Contribution

Conceptualization: SHA; Methodology: MS, KA, NF, AS, SF, KG; First draft: MS, KA; Final draft and review: SHA, KG, TA; Supervision: SHA, KA, TA; Funding acquisition: KA, SHA. All authors have read and agreed to the published version of the manuscript.

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Data Availability

Raw transcriptomic read counts were obtained from the TCGA-PRAD cohort via the NCI Genomic Data Commons (National Cancer Institute Genomic Data Commons, 2026). All other data supporting the findings of this study are available within the paper and its Supplementary Information.

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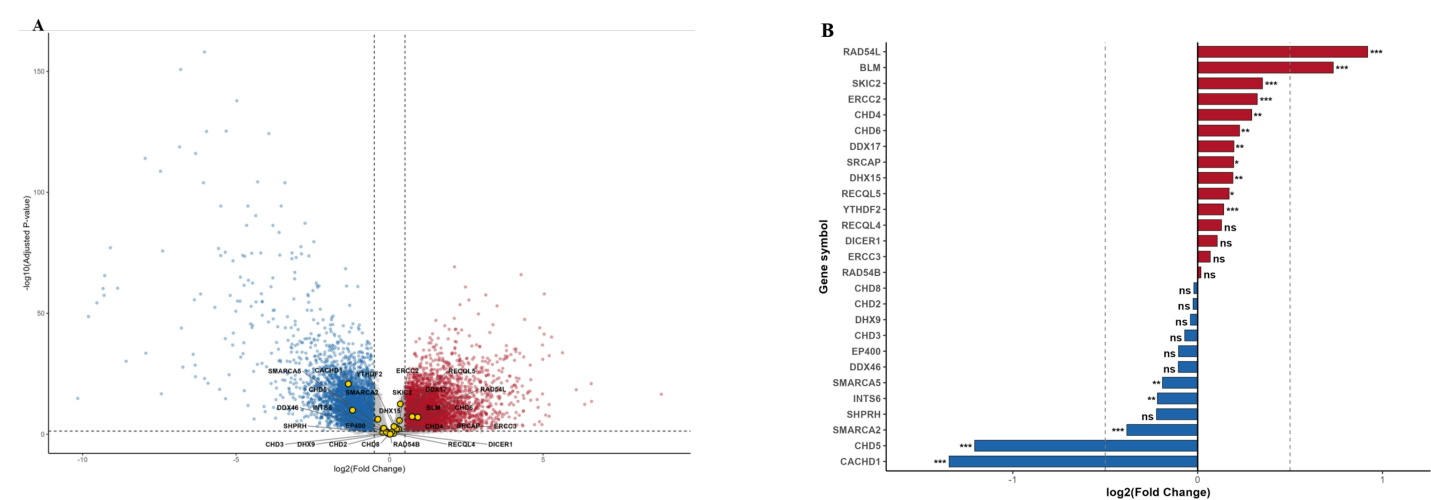
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Figures



Differential expression of helicase genes in TCGA PRAD transcriptomics data. Figure A) shows a volcano plot with significantly up-regulated (red) and down-regulated (blue) genes in PCa vs normal tissues, with the target helicase panel shown in gold; B) shows the divergent bar plot with significantly up-regulated (red) and down-regulated (blue) helicase genes in PCa vs normal tissues. B) $p_{adj} < 0.05^*$, $p_{adj} < 0.01^{**}$ and $p_{adj} < 0.001^{***}$. The figure was created in RStudio 2026.01.0 Build 392.

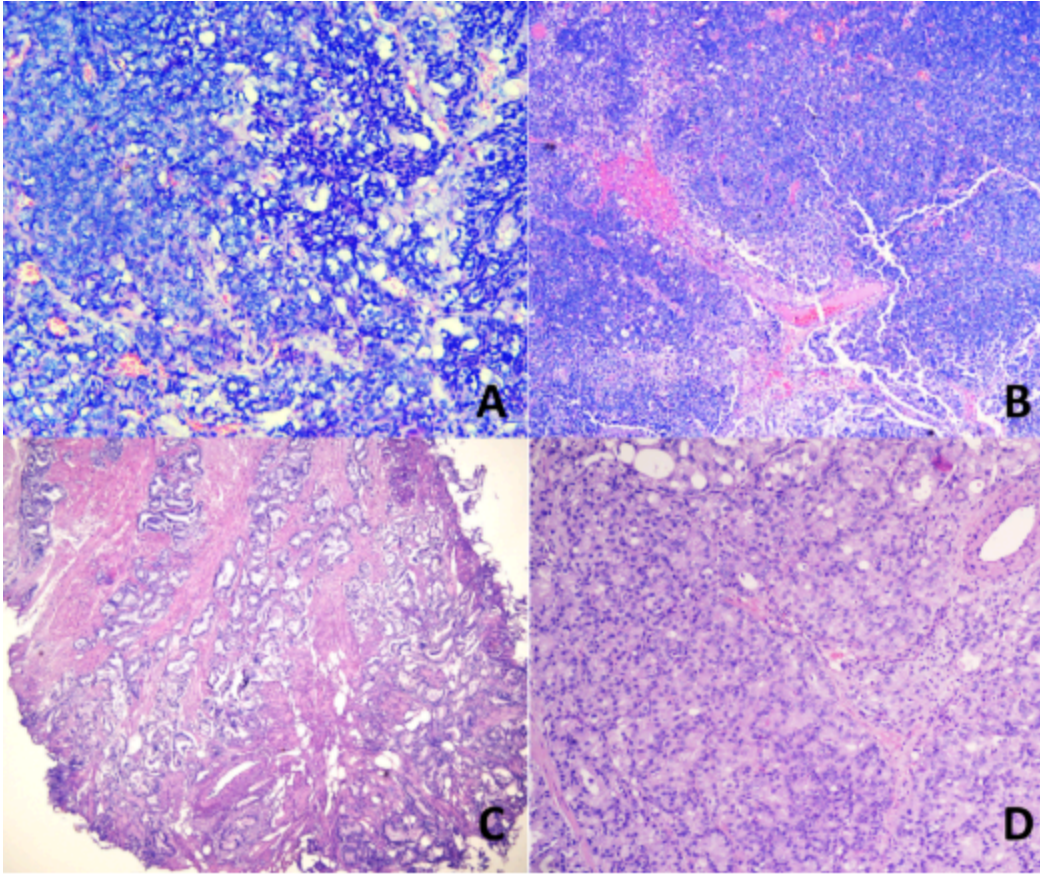


Figure 2

Representative histopathological images of EBV-negative and EBV-positive PCa tissues. The images show A) EBV-negative PCa, Gleason score of 10 (5+5) with Prognostic grade group 5 (H&E; 200X), B) EBV-positive prostatic adenocarcinoma, Gleason score of 9 (4+5), with a prognostic grade group 5 (H&E; 40X), C) EBV-negative prostatic adenocarcinoma, Gleason score of 7 (4+3), with a prognostic grade group 3 (H&E; 40X) and D) EBV-positive prostatic adenocarcinoma, Gleason score of 8 (4+4) with prognostic grade group 4 (H&E; 100X).

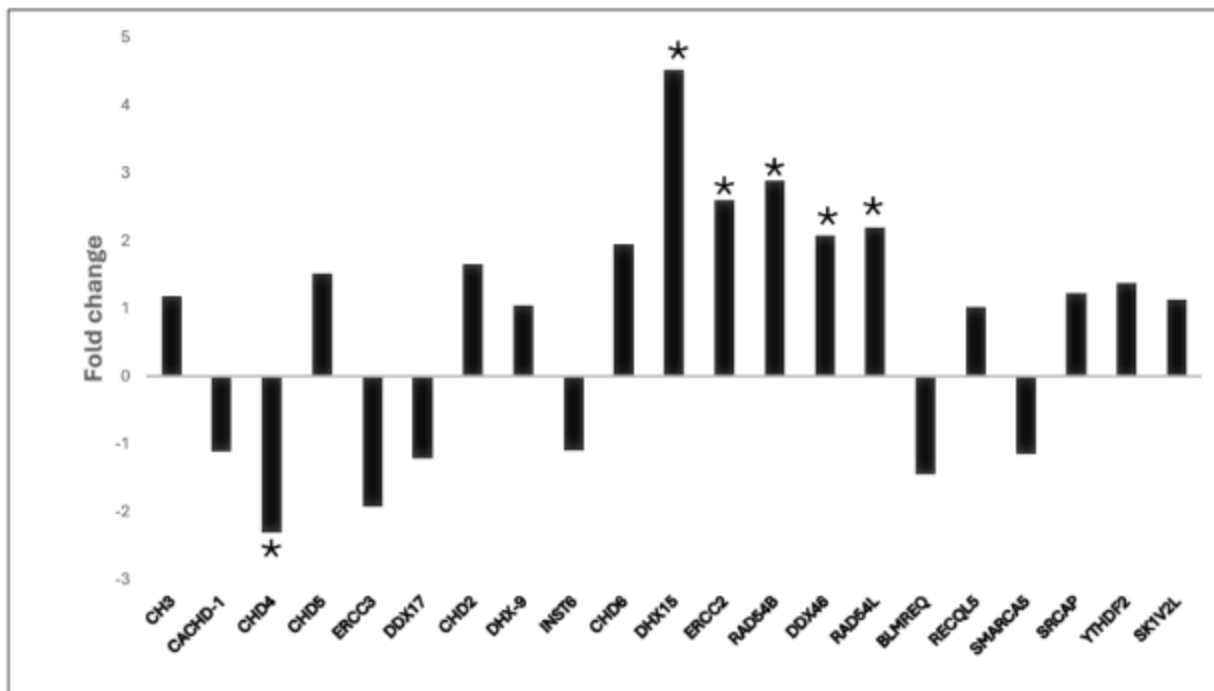


Figure 3

Differential gene expression (fold change) of selected helicase genes in EBV-positive and -negative PCa tissues. Figure shows expression of *CH3*, *CACHD-1*, *CHD4*, *CHD5*, *ERCC3*, *DDX17*, *CHD2*, *DHX9*, *INST6*, *CHD6*, *DHX15*, *ERCC2*, *RAD54B*, *DDX46*, *RAD54L*, *BLMREQ*, *RECQL5*, *SMARCA5*, *SRCAP*, *YTHDF2*, & *SKIV2L*. Genes exhibiting more than a two-fold difference in both directions are indicated by *. The figure was created in MS Excel.

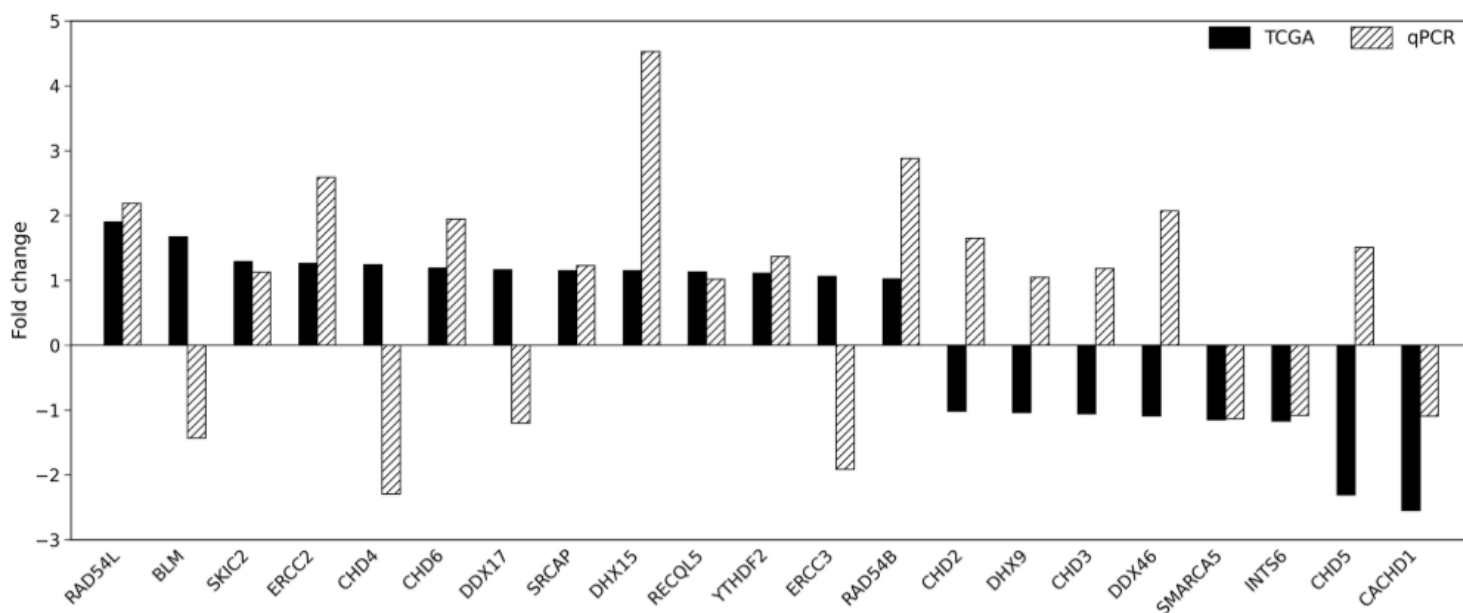


Figure 4

Comparative analysis of helicase genes in TCGA-PRAD data and qPCR data from EBV-positive and EBV-negative PCa tissues. The figure shows gene expression in FC, where black bars indicate TCGA fold change, while hatched bars indicate qPCR fold change. Both datasets share a common y-axis, with positive values indicating upregulation and negative values indicating downregulation. The figure was created in MS Excel.

Supplementary Files

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- [SupplementaryFigure1.docx](#)