Research article

Pan-cancer identified ARPC1B as a promising target for tumor immunotherapy and prognostic biomarker, particularly in READ

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ABSTRACT

ARPC1B encodes the protein known as actin-related protein 2/3 complex subunit 1 B (ARPC1B), which controls actin polymerization in the human body. Although ARPC1B has been linked to several human malignancies, its function in these cancers remains unclear. TCGA, GTEx, CCLE, Xena, CellMiner, TISIDB, and molecular signature databases were used to analyze ARPC1B expression in cancers. Visualization of data was primarily achieved using R language, version 4.0. Nineteen tumors exhibited high levels of ARPC1B expression, which were associated with different tumor stages and significantly affected the prognosis of various cancers. The level of ARPC1B expression substantially connected the narrative of ARPC1B expression with several TMB cancers and showed significant changes in MSI. Additionally, tolerance to numerous anticancer medications has been linked to high ARPC1B gene expression. Using Gene Set Variation Analysis/ Gene Set Enrichment Analysisanalysis and concentrating on Rectum adenocarcinoma (READ), we thoroughly examined the molecular processes of the ARPC1B gene in pan-cancer. Using WGCNA, we examined the co-expression network of READ and ARPC1B. Meanwhile, ten specimens were selected for immunohistochemical examination, which showed high expression of ARPC1B in READ. Human pan-cancer samples show higher ARPC1B expression than healthy tissues. In many malignancies, particularly READ, ARPC1B overexpression is associated with immune cell infiltration and a poor prognosis. These results imply that the molecular biomarker ARPC1B may be used to assess the prognosis and immune infiltration of patients with READ.

1. Introduction

A significant concern for human health has been the rise of cancer as the primary cause of death in many nations over the past several decades. Surgery, chemotherapy, radiation, immunotherapy, and targeted therapy are the cancer-directed treatment options [1]. Immunotherapy, one among these, has revolutionized cancer treatment [2] and has evolved into the fourth tumor treatment strategy after surgery, chemotherapy, and radiation. In 2013, the journal Science listed tumor immunotherapy as one of the top ten

scientific breakthroughs [3]. Although multiple cancer types show sustained clinical benefits from immunotherapy, the response rates are limited, and the underlying mechanisms are unclear. At present, there is an urgent need for clearer biomarkers in tumor immunotherapy as targets or indicators for detection and evaluation to achieve precise treatment goals.

The actin-related protein 2/3 complex (Arp 2/3 complex), which controls actin polymerization in cells, is made up of a component encoded by the ARPC1B gene. Arp2 and Arp3 are two of the seven subunits that comprise the Arp 2/3 complex, together with p16-Arc, p20-Arc, p21-Arc, p34-Arc, and p41-Arc (Arpc1b) [4,5]. According to earlier research, the prevalence, development, treatment sensitivity, and prognosis of several tumor types are significantly associated with ARPC1B [6–9]. However, the predictive value of ARPC1B across tumors has not been thoroughly studied, and its role in many cancers remains unknown. In addition, no studies have been conducted on the relationship between READ and ARPC1B expression.

Pan-cancer analyses can aid in identifying the distinctive and common traits of human malignant tumors and offer new suggestions for the clinical management of cancers [10,11]. In addition, pan-cancer analyses can be used to identify beneficial prognostic indicators [12–14]. Pan-cancer analysis is crucial for identifying new diagnostic biomarkers and creating more potent molecular targets for cancer treatment. However, the role of ARPC1B in human cancers remains largely unknown.

The current study carefully analyzed the prognosis of patients and the expression of ARPC1B in 33 different cancers. Additionally, we examined the association between tumor immunity and ARPC1B expression levels. Our research demonstrates that ARPC1B may play a role in several tumors, notably READ, and may be a prognostic biomarker linked to immune infiltration. The technical approach of this study is shown in Fig. 1.

2. Materials and methods

2.1. TCGA data gathering and difference analysis

The central repository for information on cancer genes is the TCGA database, which includes gene expression profiles, nucleotide sequence variations, SNP, and other data. We retrieved 33 cases of pan-cancerous tumors, including mRNA expression, and SNP data for further research. Gene expression data for each tissue were obtained from the GTEX database, adjusted and combined with TCGA data to identify variations in gene expression among tumors. Data from every tumor cell line were collected from the CCLE database to explore the connection between tumor staging and presentation. Gene expression levels within those tumor tissues were then assessed based on the tissue source.

2.2. Analysis of prognostic correlation

Information on the progression-free survival (PFI) and overall survival (OS) of TCGA patients was retrieved from the Xena database to better comprehend the connection between gene expression and patient outcomes. Survival studies for each cancer type was conducted using the Kaplan–Meier technique (P < 0.05), and the 'survival' and 'survminer' packages were used to assess the results. Further investigation of the connection between survival and expression of the gene was done using Cox analysis using the 'forest plot'
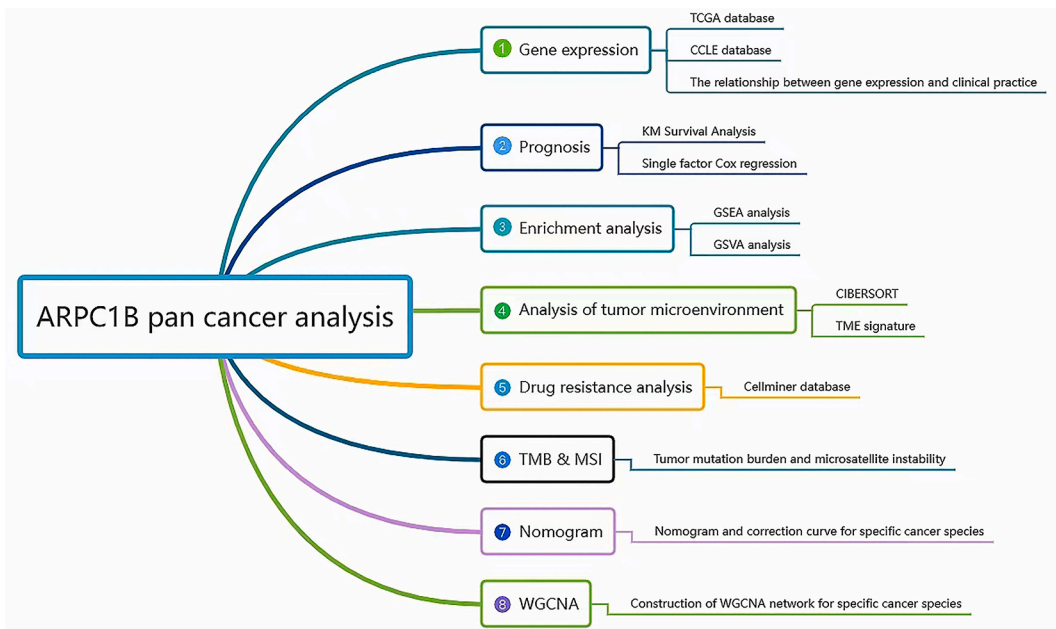

Fig. 1. Technical approach of ARPC1B pan-cancer analysis.

and 'survival' packages.

2.3. Study on immune cell infiltration

The ratio of immune-infiltrating cells was calculated from the RNA-seq data of 33 individuals living with cancer using the CIBERPORT technique. The association between the resistant cell content and expression levels was also examined. Additionally, the TISIDB website investigated possible connections between immunomodulatory elements and gene expressions, including chemokines, cyclosporine, immunostimulators, and MHC molecules.

Fig. 2. Pan-cancer expression analysis of ARPC1B gene. **A** The expression of ARPC1B in 33 human cancers was analyzed using TCGA and GTEX data sets. **B** The expression of ARPC1B in different tumor cell lines in CCLE expression profile. **C** Association between TREM2 expression and tumor stage in ACC, BLCA, COAD, KIRC, and LUAD.

2.4. Drug sensitivity testing

The CellMiner database is based on 60 cancer cells identified by the National Cancer Institute (NCI) Cancer Research Center. The most prevalent cancer cell line used to evaluate anticancer drugs was the NCI-60 cell line. RNA sequencing gene expression data and NCI-60 drug sensitivity information were retrieved to perform a correlation study (P < 0.05) to examine the relationship between genes and sensitivity to common anticancer drugs.

2.5. GSVA enrichment analysis

The enrichment of the transcript gene sets was assessed using a non-parametric unsupervised technique known as Gene Set Variation Analysis (GSVA). The target gene set was comprehensively evaluated using GSVA, which translates gene-level alterations into pathway variations and evaluates the biological function of the sample. Gene sets were obtained from the MSigDB (v7.0).
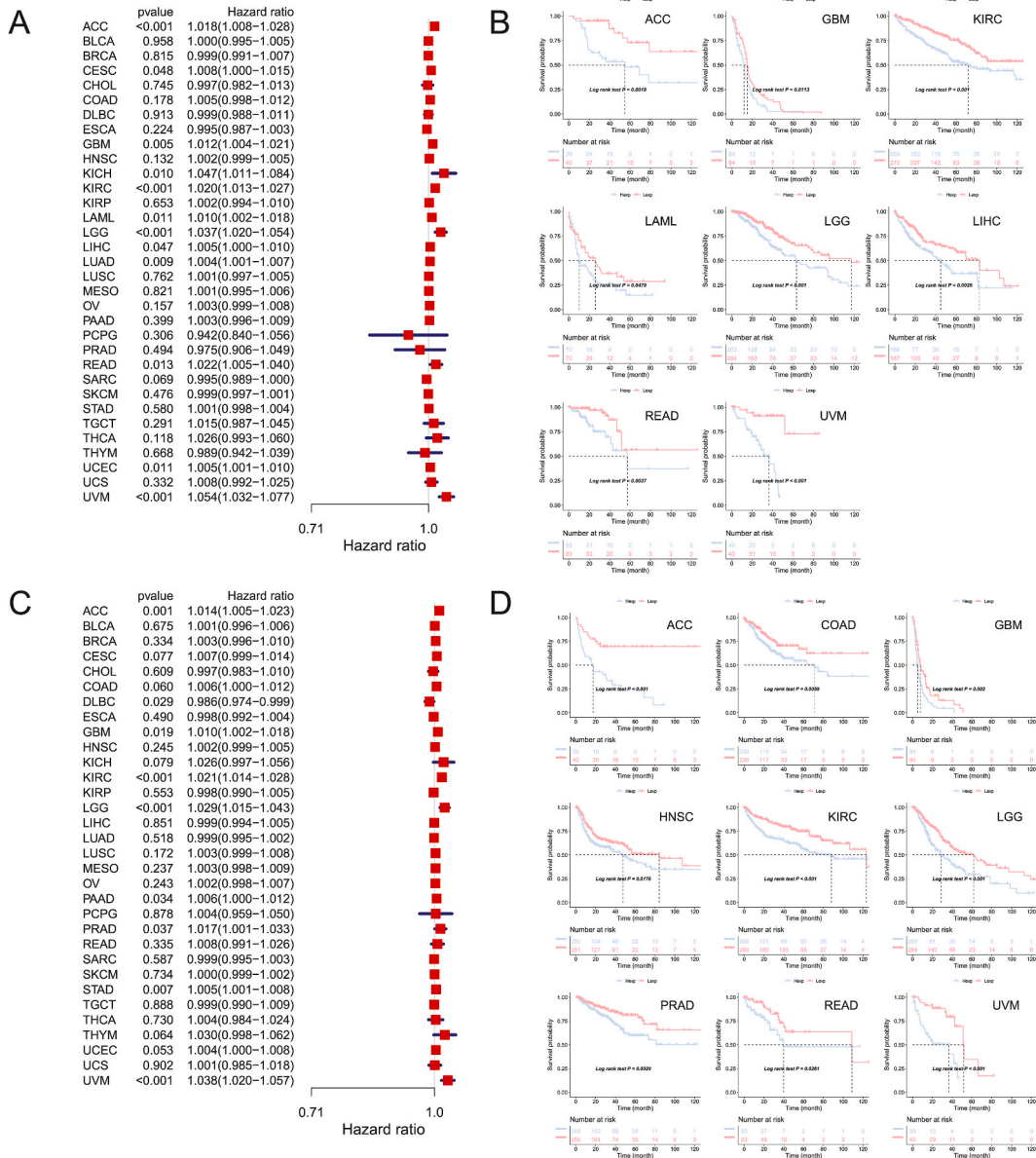

Fig. 3. A Association between ARPC1B expression and overall survival time in days (OS). **B** Kaplan–Meier analysis of the association between ARPC1B expression and OS. **C** Association between the ARPC1B expression and PFI of cancer patients. **D** Kaplan–Meier analysis of the association between ARPC1B expression and PFI.

2.6. GSEA enrichment analysis

Genes were sorted using Gene Set Enrichment Analysis (GSEA) based on the degree of altered expression in both sample types. A sorting table was used to assess whether a specific set of genes was enriched at the front or bottom of the sorting tables. The 'cluster profile' and 'enrich plot' software programs were used to assess GSEA. The potential biological basis for survival disparities in 33 cancer patients was examined to understand the signaling pathway differences between the elevated and decreased gene expression groups.

2.7. TMB and MSI data analysis

Tumor mutational burden (TMB) measures the number of somatic gene-coding mistakes, base deletions, insertions, or substitutions discovered per million bases. TMB was calculated by dividing the non-synonymous mutation site by the entire length of the protein nucleotide sequence. The variable frequency variation/exon length for each tumor sample was considered during TMB calculation. The microsatellite instability (MSI) level for each TCGA patient was calculated based on previously published studies [15].

2.8. Analysis

The R software was used to perform all statistical analyses (version 4.0). Hazard ratios and 95% confidence intervals (CI) were calculated using univariate survival analysis. –Kaplan–Meier analysis was used to analyze patient survival according to the degree of gene regulation. Statistical significance was set at $P < 0.05$ (two-sided).
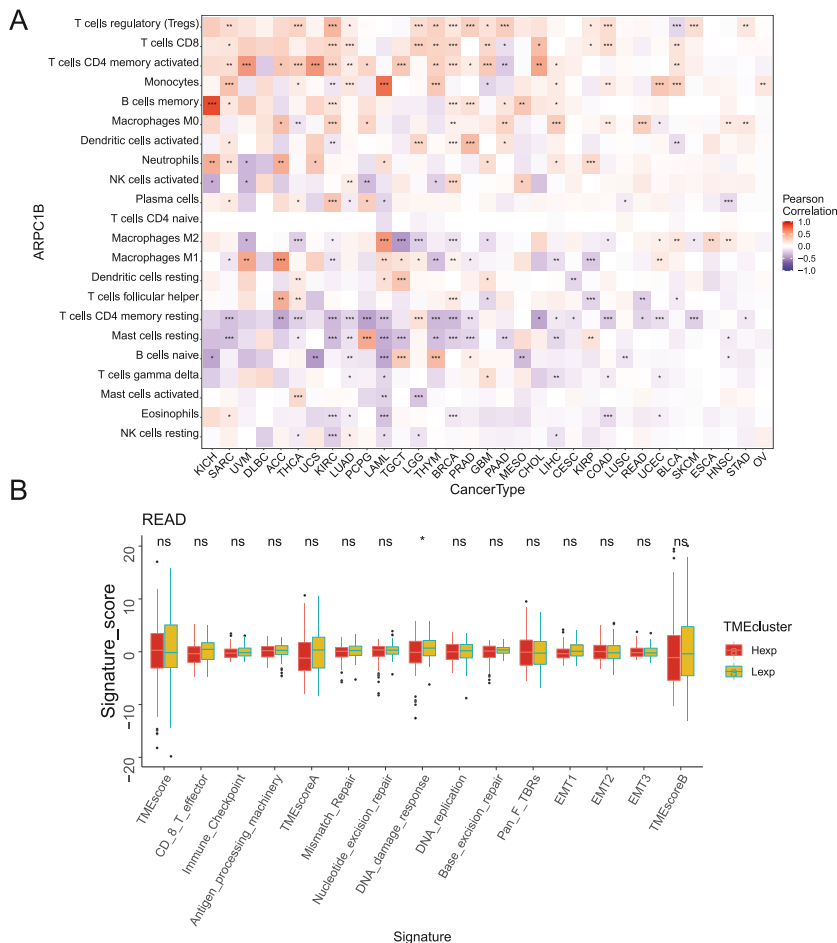

Fig. 4. A Association between ARPC1B expression and overall survival time in days (OS). **B** Kaplan–Meier analysis of the association between ARPC1B expression and OS.

3. Result

3.1. Analysis of ARPC1B gene expression across cancer types

The expression of ARPC1B was analyzed using TCGA and GTEX datasets to examine 33 human malignancies. According to the findings, 19 cancers strongly express the gene, including the BLCA, CESC, CHOL, COAD, ESCA, GBM, HNSC, KIRC, KIRP, LGG, LIHC, LUAD, OV, PAAD, READ, SKCM, STAD, TGCT, and UCEC (Fig. 2A). Most normal tissues express ARPC1B at lower levels than cancerous tissues. The figure shows the expression of ARPC1B in several tumor cell lines according to the CCLE expression profile (Fig. 2B).
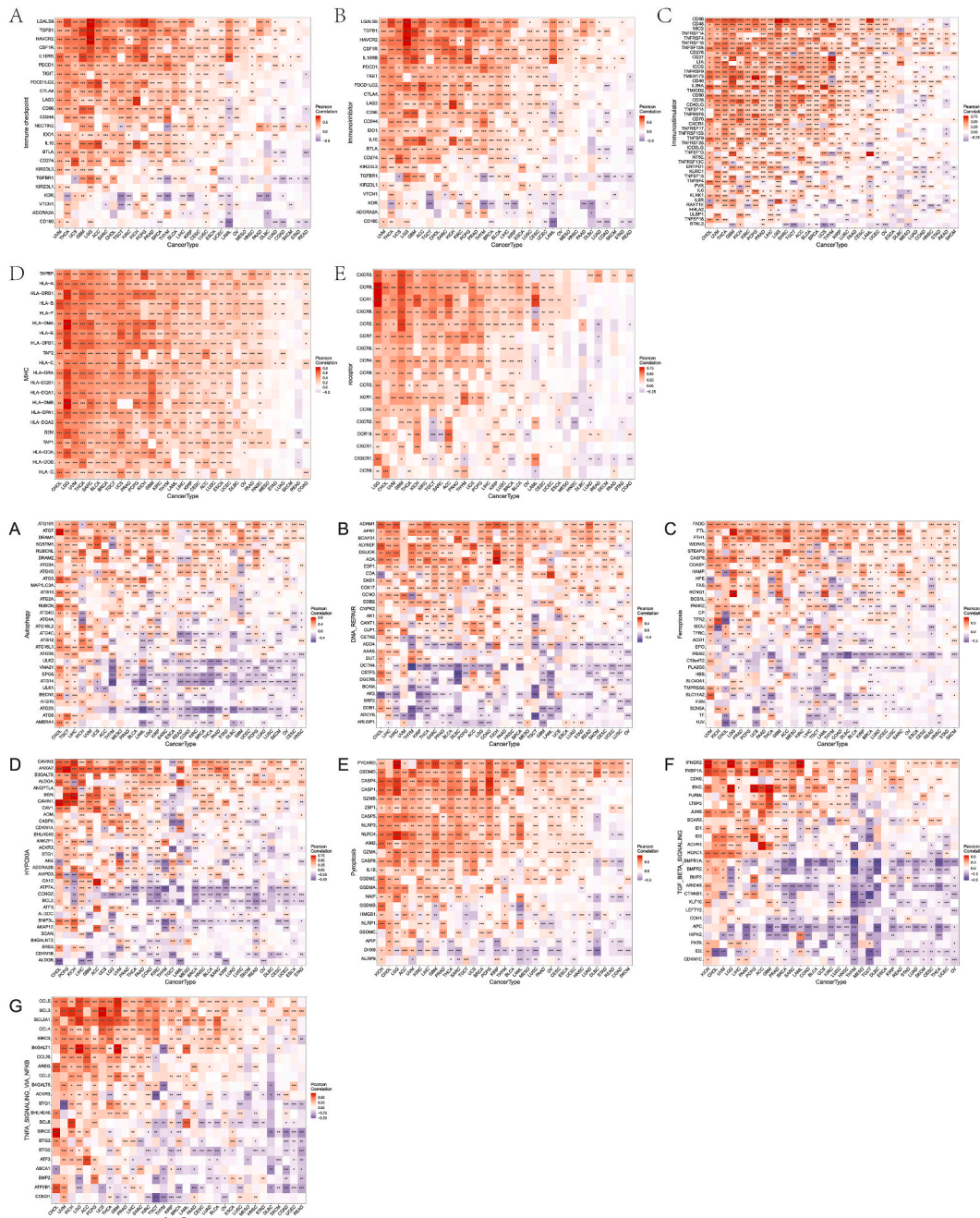

Fig. 5. The relationship between the expression of 33 tumor immune-related genes and ARPC1B was further studied by G gene co-expression analysis. **A** The ARPC1B expression significantly correlated with the infiltration levels of nearly all innate immunity genes. **B** The ARPC1B expression highly correlated with the common tumor-related regulatory genes.

Several tumor stages, including ACC, BLCA, COAD, KIRC, and LUAD, were correlated with ARPC1B. (Fig. 2C). We evaluated the association between cancer prognosis and ARPC1B expression using OS and PFI as survival markers. The findings demonstrated that in 12 cancer types with ACC, CESC, GBM, KICH, KIRC, LAML, LGG, LIHC, LUAD, READ, UCEC, and UVM, ARPC1B expression was significantly correlated with OS (Fig. 3A). Additionally, KM plot survival analysis revealed that high expression of ARPC1B links to poor OS in eight different cancers, including ACC, GBM, KIRC, LAML, LGG, LIHC, READ, and UVM (Fig. 3B). In nine cancer types, including ACC, DLBC, GBM, KIRC, LGG, PAAD, PRAD, STAD, and UVM, ARPC1B expression strongly correlated with PFI (Fig. 3C). High expression of ARPC1B was associated with worse PFI in patients with nine different types of cancer, including ACC, COAD, GBM, HNSC, KIRC, LGG, PRAD, READ, and UVM, according to findings of KM plot survival analysis (Fig. 3D).

3.2. Pan-cancer expression and immune infiltration

The tumor microenvironment is composed of the extracellular matrix, various growth hormones, inflammatory agents, and unique physical and chemical properties, with cancer cells constituting the majority. This microenvironment substantially affects tumor diagnosis, survival rate, and treatment sensitivity. Our findings indicated that immune infiltration closely correlated with the expression of ARPC1B. Specifically, 15 cancers were related to T cell regulatory (Treg) cells, 12 to T cells CD8, and 17 to CD4 memory-activated T cells (Fig. 4A). Rectal cancer tumor microenvironment analysis revealed a substantial correlation between DNA damage response score and disease (Fig. 4B).

3.3. Pan-cancer expression and key regulatory genes

Gene co-expression analysis was used to further investigate the link between the expression of 33 tumor immune-related genes and ARPC1B expression. The genes examined were MHC, immune activators, immunosuppressive factors, chemokines, and chemokine receptor proteins. The findings showed that ARPC1B was a relevant authority for nearly all innate immunity genes (Fig. 5A). The common tumor-related regulating genes TGF beta signaling, TNFa signaling, hypoxia, scorch death, DNA repair, autophagy gene, and iron death-related gene are also highly connected with ARPC1B. (Fig. 5B).

3.4. Pan-cancer expression and TMB and MSI

TMB and MSI are two new biomarkers for the effectiveness of immunotherapies. This study investigated the association between ARPC1B and TMB expression, and observed an association between the expression level of ARPC1B and a range of TMB cancers, including COAD, UCS, LUAD, ACC, KIRC, OV, and KIRP (Fig. 6A). MSI revealed significant variations in ARPC1B expression in SKCM, PRAD, COAD, BRCA, THCA, TGCT, and DLBC cells (Fig. 6B).

3.5. Pan-cancer expression and drug sensitivity

Surgery and chemotherapy clearly demonstrate therapeutic benefits for early stage tumors. We assessed the association between gene expression and pharmaceuticals and explored the relationship between ARPC1B and popular anticancer medications using the CellMiner database, and found that high ARPC1B expression was associated with the ability to tolerate a range of anticancer medications (Fig. 7). Calusterone, PD-98059, XL-147, Ixazomib citrate, Trametinib, Bafetinib, Cobimetinib, Selumetinib, ABT-199, Hypothemycin, Vemurafenib, and Dabrafenib were all favorably associated with ARPC1B, whereas docetaxel had a negative
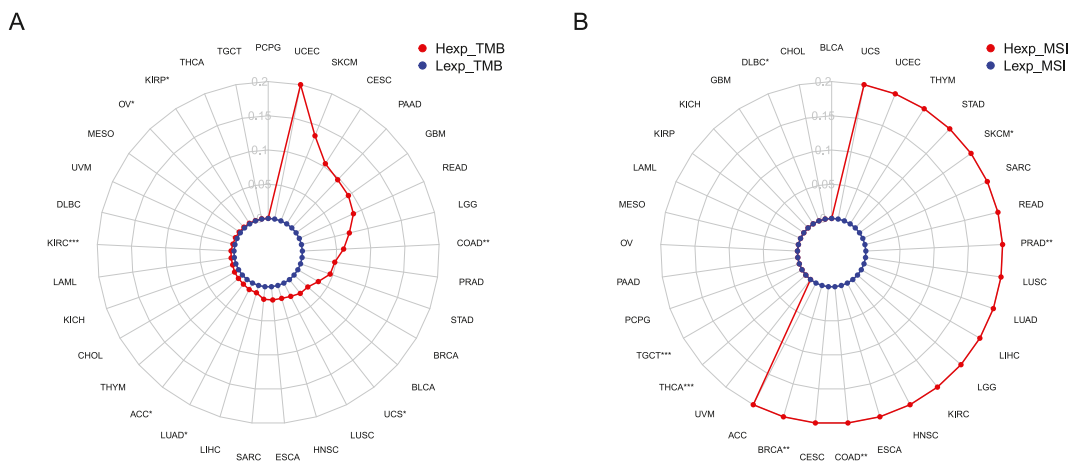

Fig. 6. Correlation between the HSF1 gene expression and TMB and MSI in pan-cancer. **A** Shows the association between the expression level of ARPC1B and a range of TMB cancers. **B** Shows the association between the ARPC1B gene expression and MSI in diverse tumors.
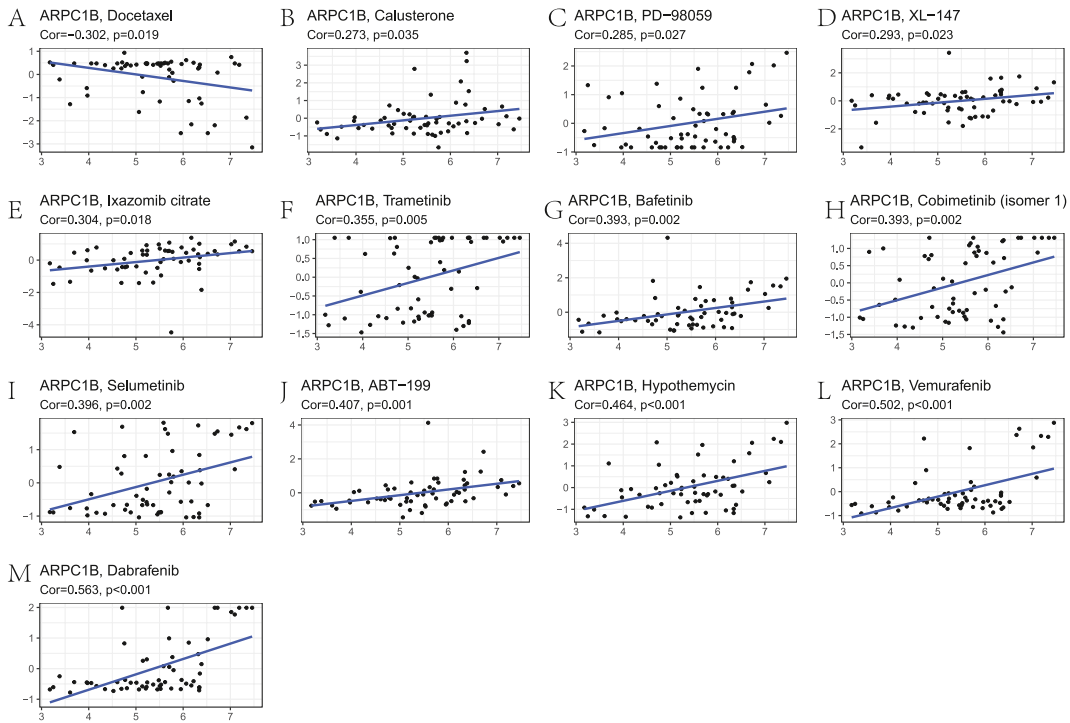
Fig. 7. A–M The relationship between the ARPC1B gene and popular anticancer drugs was explored using the CellMiner database.

correlation.

3.6. Pan-cancer expression and GSVA/GSEA

To classify the samples into high- and low-expression groups based on the median gene expression in each tumor, we first scored all tumors with GSVA to thoroughly investigate the molecular mechanism of ARPC1B in pan-cancer. The findings demonstrated that the elevated expression of ARPC1B in rectal cancer was mainly focused on the signaling pathways for HEDGEHOG_SIGNALING, UV_RESPONSE_UP, REACTIVE_OXYGEN_ SPECIES_PATHWAY, NOTCH_SIGNALING, and WNT_BETA_CATENIN_Signaling (Fig. 8A). The figure displays the results of the GSEA analysis of rectal cancer tissues and ARPC1B. (Fig. 8B).

3.7. WGCNA analysis

We further constructed a WGCNA network based on READ target respondents' data to investigate the co-expression system associated with ARPC1B in READ. The soft level is considered six by the function "SFT $powerestimate," determining the soft
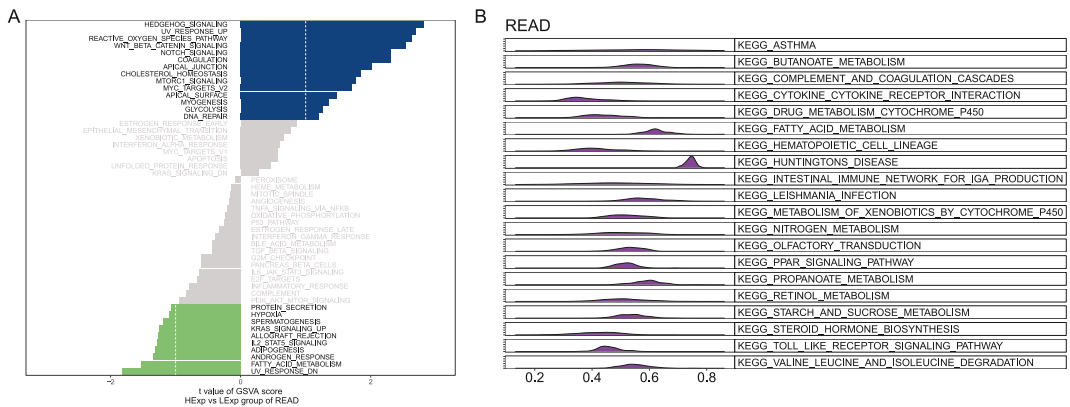

Fig. 8. A GSVA score showed the pathway of elevated expression of ARPC1B in rectal cancer. **B** The figure displays the results of the GSEA analysis of tissues from rectal cancer and ARPC1B.

threshold. Based on the Tom matrix, 16 gene modules were identified in this investigation. Black (510), blue (1830), brown (702), cyan (91), green (284), green-yellow (105), green (171), green 60 (57), light cyan (59), magenta (195), midnight blue (86), pin (211), purple (139), salmon (92), tan (97), and yellow constituted the colors (371). According to subsequent research, the blue module exhibited the strongest correlation between quality and modules (cor = 0.43, P = (4e 09)) (Fig. 9A). We also used the blue gene module for pathway analysis. According to the GO data, the gene was highly enriched in pathways related to Golgi vesicle transport, protein catabolism, protein targeting, and other functions (Fig. 9B). According to the KEGG data, the genes were mostly enriched in pathways for carbon metabolism, pathogenic *Escherichia coli* infection, and amino acid synthesis (Fig. 9C).

3.8. ARPC1B risk and independent prognosis analysis

The nomogram prediction model was built based on the expression of ARPC1B and symptoms, and the regression analysis findings were presented as a nomogram. Logistic regression analysis demonstrated that in the READ sample, the expression of ARPC1B significantly increased the predictive power of the model (Fig. 10A). The model impact was constant, and this study draws correction curves for three-years and five-years simultaneously (Fig. 10B).
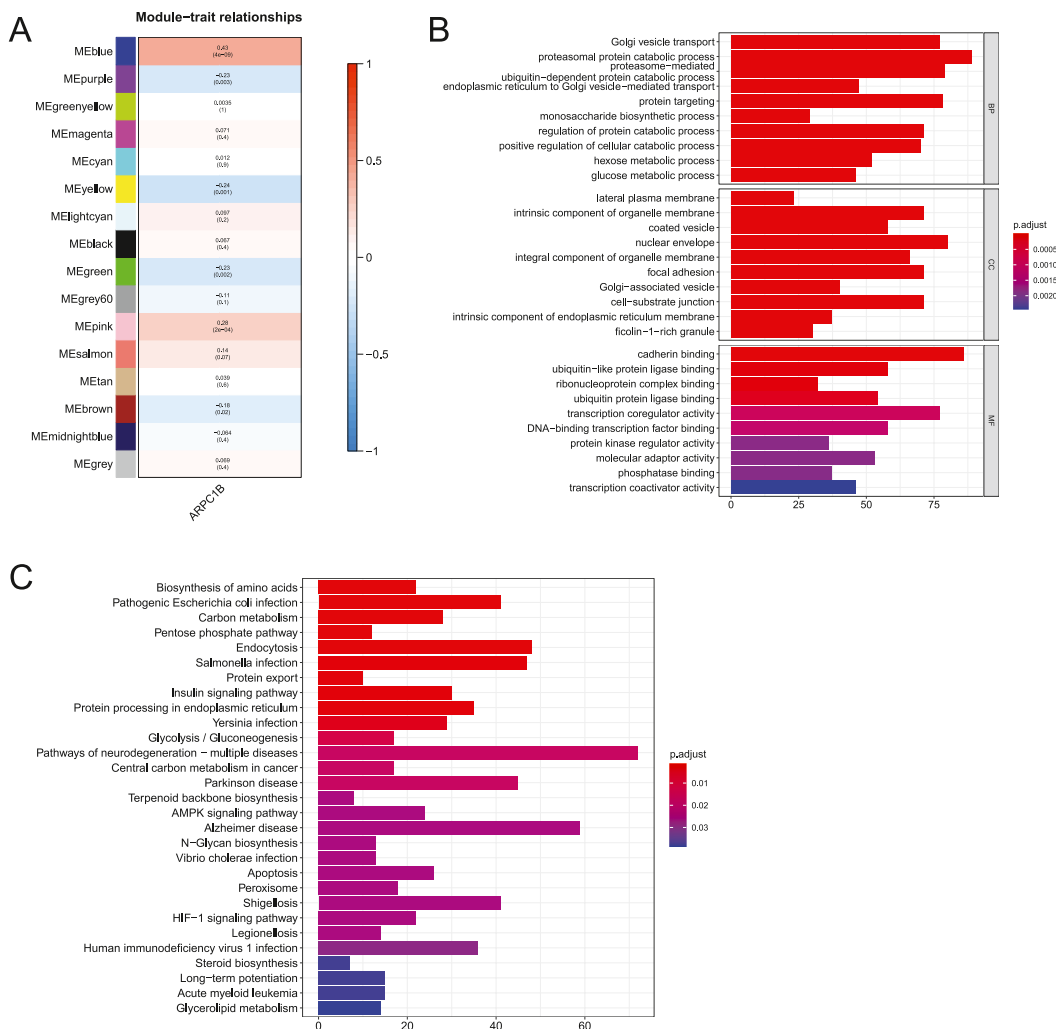

Fig. 9. A WGCNA network is constructed based on the data of READ target respondents to study ARPC1B-related co-expression systems in READ. **A** Based on the Tom matrix, 16 gene modules were found in this investigation. The blue module exhibited the strongest correlation between qualities and modules (cor = 0.43, P = (4e 09)). **B** According to the GO data, the gene was highly enriched in pathways for Golgi vesicle transport, protein catabolism, protein targeting, and other functions. **C** According to KEGG data, the genes were mostly enriched in pathways for carbon metabolism, pathogenic *Escherichia coli* infection, and the synthesis of amino acids. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)
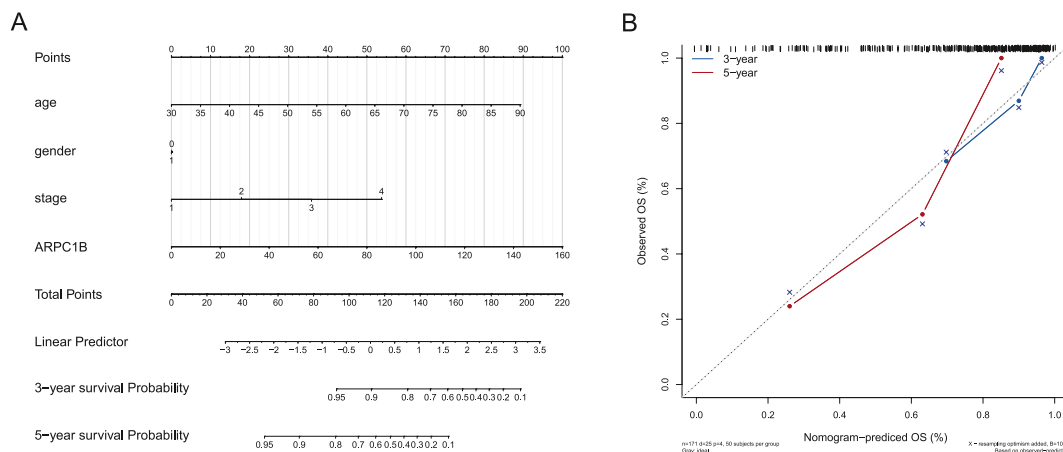
Fig. 10. The nomogram prediction model was constructed based on the expression of the ARPC1B gene and symptoms, and the regression analysis findings are presented as a nomogram. **A** The outcomes of logistic regression analysis demonstrated that, in the READ sample, the expression of ARPC1B gene significantly increased the model's predictive power. **B** Three-years and five-years correction curves were plotted based on constant model effects.

3.9. Differential expression of ARPC1B between READ and rectal normal tissue samples

To evaluate ARPC1B expression at the protein level, we analyzed ten specimens, including five normal rectal tissues and five rectal adenocarcinoma tissues. Normal rectal tissues showed low ARPC1B expression, whereas rectal adenocarcinoma tissues exhibited high ARPC1B expression (Fig. 11).

4. Discussion

In this study, we examined the expression of ARPC1B in 33 human malignancies using TCGA and GTEX datasets, highlighting the precise distinction in pan-cancer ARPC1B expression between tumors and normal tissues. The findings showed that 19 cancers, including BLCA, CESC, CHOL, COAD, ESCA, GBM, HNSC, KIRC, KIRP, LGG, LIHC, LUAD, OV, PAAD, READ, SKCM, STAD, TGCT, and UCEC, exhibited significant gene expression (Fig. 2A). Most normal tissues express ARPC1B at lower levels than cancerous tissues. The Figure shows the presence of ARPC1B in several tumor cell lines according to the CCLE expression profile (Fig. 2B). Additionally, the stages of several malignancies, including ACC, BLCA, COAD, KIRC, and LUAD, were associated with ARPC1B expression (Fig. 2C). In summary, our findings support earlier research indicating that aberrant ARPC1B expression may be a critical factor in carcinogenesis, and offer new information for further investigation into the function of ARPC1B in cancer.

The human ARPC1B gene is linked to the actin protein, which produces the protein known as 2/3 complex subunit 1 B. The seven subunits that comprise the Acp 2/3 complex are Arp2, Arp3, Arpc1, Arpc2, Arpc3, Arpc4, and Arpc5 [4–6]. ARPC1B regulates the actin
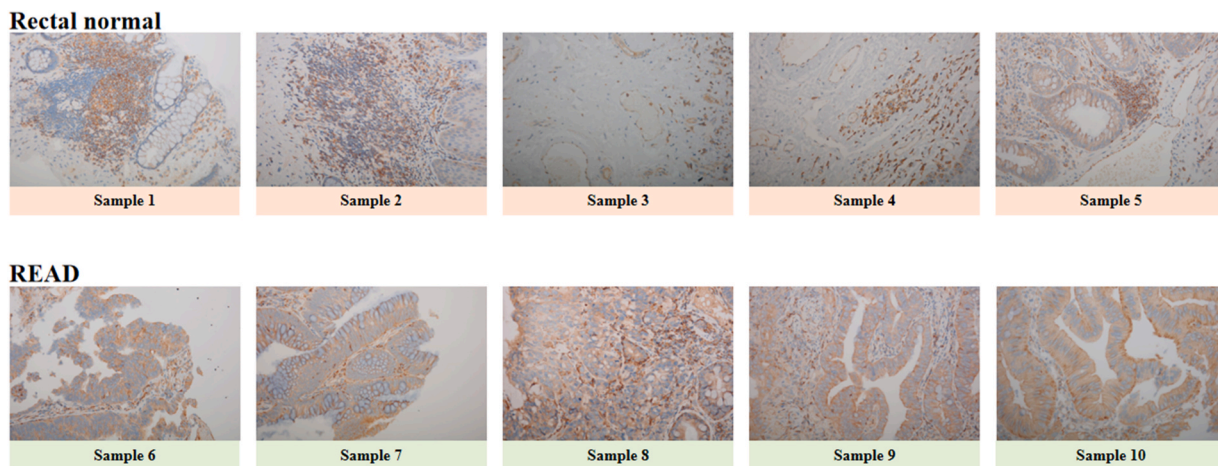

Fig. 11. Immunohistochemical images of ARPC1B gene expression between normal rectal tissue (Sample 1–5) and READ tissue (Sample 6–10). The expression of ARPC1B protein in rectal adenocarcinoma (READ) was significantly higher than that in normal tissues.

polymerization process, contributing to the stability of actin filaments, formation of microfilaments from actin monomers, and promotion of cell motility. Actin filaments are crucial for the development of the cytoskeleton of cells, establishment of cell-cell junctions, and movement of several pathogens [16,17]. Various studies have shown that ARPC1B is closely related to the occurrence, development, treatment sensitivity, and prognosis of a variety of tumors [8–11].

The expression levels of ARPC1B are reduced or abnormally methylated in a variety of human tumors, including gastric cancer, osteosarcoma, non-small cell lung cancer, and oral squamous cell carcinoma [9,18–23]. High ARPC1B expression is linked to advanced malignancy, poor outcomes, and TAM infiltration [24]. Overexpression of ARPC1B is also associated with breast cancer and radiation-resistant intraocular choroidal melanoma cells, enhancing tumorigenicity. The precise mechanism of ARPC1B and tumorigenesis is not clear; while overexpression may influence cell migration, the reduced expression of this gene is related to dysplastic morphology [25]. However, to the best of our knowledge, no research has been published on the relationship between READ and ARPC1B expression, and the underlying mechanism remains unknown.

The tumor microenvironment is a complex and dynamic cellular microenvironment. Every element in this environment can induce malignant transformation of tumors, accelerate tumor occurrence and development, and protect tumors from the host immune system [26–28]. Although immunotherapy has made significant advances in cancer treatment, several barriers remain to its widespread use. Therefore, the discovery of new targets and biomarkers is critical to increase the efficacy of immunotherapy. Thoroughly understanding the status of immune infiltration in cancer patients is critical for selecting the best customized immunotherapy strategy [2, 28]. According to previous studies, ARPC1B is significantly correlated with immunosuppressors and immunological inhibitory checkpoints creating an immunosuppressive microenvironment [29,30]. To investigate the immune status of cancer patients, we examined the expression of ARPC1B and discovered a connection between ARPC1B and tumor immune cells. Gene co-expression networks can serve various purposes, including prioritization of candidate disease genes, functional gene annotation, and identification of regulatory genes [31]. The link between the expression of 33 tumor immune-related genes and ARPC1B was further investigated using gene co-expression analysis. The findings showed that ARPC1B was strongly associated with almost all immune-related genes. ARPC1B's strong associations with common tumor-related regulatory genes such as TGF beta signaling, TNFa signaling, hypoxia, scorch death, DNA repair, autophagy gene, and iron death-related gene provide additional evidence supporting its potential as a tumor immunological biomarker.

TMB and MSI are two new biomarkers of the immunotherapeutic response. The standard definition of TMB is the total number of somatic non-synonymous mutations per megabase (Mut/Mb), which includes frameshift mutations, insertions, point mutations, and deletions [32–34]. Initiation of these mutations involves the production of aberrant proteins that function as neoantigens and trigger antitumor immune responses (Fig. 2) [35]. MSI has been linked to dMMR and is thought to be a potentially helpful prognostic biomarker of ICI response [36]. MSI, in particular, causes the accumulation of mutations, which results in the creation of neoantigens and activation of antitumor immune responses [37,38]. In this study, we examined the relationship between TMB and ARPC1B expression. Researchers have discovered a strong association between ARPC1B expression and various TMB cancers, including COAD, UCS, LUAD, ACC, KIRC, OV, and KIRP. Significant differences in ARPC1B expression in SKCM, PRAD, COAD, BRCA, THCA, TGCT, and DLBC were observed according to MSI. These data demonstrate a strong correlation between ARPC1B modifications and TMB and MSI levels across different cancer types, indicating that ARPC1B abnormalities may serve as biomarkers for tumor therapy.

CallMiner is a database of genomic and pharmaceutical tools used to identify drug patterns and transcripts in the NCI-60 cell line [39]. Our study discovered a correlation between ARPC1B pan-cancer analysis and the anticancer drug sensitivity using CellMiner, including various antitumor drugs such as calusterone. Calusterone showed a positive correlation with PD-98059, XL-147, Ixazomib ciltrate, Trametinib, Bafetinib, Cobimetinib, Selumetinib, ABT-199, Hypothemycin, Vemurafenib, and Dabrafenib. However, the expression of ARPC1B had a strong inverse correlation with drug susceptibility to docetaxel. To explore tumor therapy possibilities and guard against tumor resistance, we examined the association between pan-cancer analysis of ARP1CB and sensitivity to anticancer medications.

GSVA is an unsupervised GSE technique that calculates variations in pathway activity across a sample population. GSEA was used to examine the difference in the behavior of genes between the two groups. GSVA builds on GSEA, characterizing a set of genes by two condition groups defined in the sample. We used GSVA to score all cancers, and the median gene expression of each tumor to split the samples into groups with high and low-expression, because the molecular basis for the involvement of ARPC1B gene in pan-cancer is unknown. The results showed that in rectal cancer, the high expression of ARPC1B was primarily focused on the HEDGEHOG_SIGNALING, UV_RESPONSE_UP, REACTIVE_OXYGEN_SPECIES_PATHWAY, NOTCH_SIGNALING, WNT_BETA_CATENIN_Signaling, and other signaling pathways.

High ARPC1B expression is associated with poor clinical outcomes in colon, breast, and lung cancers [40]. In our study, the expression of ARPC1B, including ACC, CESC, GBM, KICH, KIRC, LAML, LGG, LUAD, READ, UCEC, and UVM tumors, was closely correlated with OS in 12 patients with cancer. Furthermore, KM plot survival analysis indicated that high ARPC1B expression was related to adverse OS in eight types of cancers, including ACC, GBM, KIRC, LAML, LGG, LIHC, READ, and UVM. In nine different types of cancers, including ACC, DLBC, GBM, KIRC, LGG, PAAD, PRAD, STAD, and UVM tumors, the expression of ARPC1B was closely correlated with PFI. According to the KM plot of survival analysis, patients with nine different types of cancer, including ACC, COAD, GBM, HNSC, KIRC, LGG, PRAD, READ, and UVM, demonstrated lower PFI levels with high expression of ARPC1B. These findings imply that ARPC1B may have prognostic significance in a range of tumors.

We constructed a nomogram prediction model based on the expression of ARPC1B and clinical symptoms. The results of the regression analysis were presented in the form of a nomogram to examine ARPC1B risk and independent prognosis. Logistic regression analysis revealed that ARPC1B expression significantly contributed to the predictive efficiency of the model in READ samples. This view is supported by the consistent effect of the 3- and 5-year correction curve models.

Our analysis showed that high ARPC1B expression was associated with poor OS and was an independent prognostic factor for READ, which may serve as a valid biomarker for the prognostic assessment of READ in the clinic. Additionally, by examining the association between ARPC1B and commonly used anticancer drugs, we found that high expression of this gene may be associated with increased tolerance to a range of anticancer drugs. These findings hold promise for future clinical application. For example, measuring ARPC1B expression in the pathology of postoperative patients could serve as a reference index for screening drugs in prognostic assessment and subsequent treatment planning. Patients with high ARPC1B expression have a relatively poor prognosis, suggesting that chemotherapeutic drugs with a high sensitivity to this gene should be prioritized.

ARPC1B is a promising target for READ immunotherapy. Our study revealed a close association between the expression of ARPC1B and immune cell infiltration, including T cell regulatory (Treg) cells, CD8 T cells, CD4 memory-activated T cells, and other cells. Related studies have shown that Tregs are immunosuppressive cells capable of inhibiting the activation of tumor-resistant T cells by producing immunosuppressive cytokines and immunosuppressive CTLA4 [41]. The expression of ARPC1B can activate Tregs and inhibit the function and proliferation of T cells, leading to a lack of effective response to immune checkpoint blockade (ICB) therapy in this group of patients. Previous studies have shown that anti-MDSC therapy and Tregs depletion can reactivate T cells and improve the therapeutic efficacy of ICB [42–44]. Therefore, in future studies on READ immunotherapy, the high correlation between ARPC1B expression and Tregs suggests its potential use as an indicator for Treg depletion therapy in READ. Additionally, molecular drugs targeting ARPC1B can be explored. Owing to the mutability, immune infiltration, and prognostic relevance of ARPC1B, further investigation is warranted to determine its potential as a target for mRNA vaccines production for the treatment of READ.

Since large-scale microarray and sequencing data were initially gathered by examining tumor tissue information, a cellular-level examination of immune cell markers could have induced a systematic bias. Future research should rely on better resolution approaches such as single-cell RNA sequencing to overcome this obstacle. Second, although clinical specimens were initially included in this study for validation, the sample size was modest. Further research is needed to confirm the expression and mechanism of action of ARPC1B at the cellular and molecular levels. Finally, although we discovered that ARPC1B expression was linked to immune cell infiltration in tumors and patient survival, more prospective studies are needed to investigate the relationship between ARPC1B expression and immune cell infiltration in various cancer populations. This will help clarify the mechanism of action of ARPC1B in tumors, and guide clinical treatment protocols.

This study is remarkable in that it examined the expression of ARPC1B in cancer using a pan-cancer approach, offering new perspectives on ARPC1B research. Our findings suggest that ARPC1B is involved in the formation and prognosis of a wide range of cancers, potentially influencing the tumor microenvironment, making it a promising immunotherapeutic target and prognostic biomarker. Furthermore, we explored the relationship between READ and ARPC1B expression, which has been shown to alter the tumor microenvironment and prognosis in READ. We investigated the signaling pathways and related gene modules linked to high ARPC1B expression in READ. This lays the foundation for a deeper understanding of ARPC1B's role in READ providing insights into potential targets and prognostic biomarkers for READ immunotherapy. This study used ten specimens for immunohistochemical validation and performed bioinformatics analysis of several databases.

5. Conclusions

In conclusion, we investigated the role of ARPC1B expression in human malignancies from a pan-cancer perspective, and elucidated its prognostic and immunological importance. Our findings suggest that ARPC1B may serve as an immunotherapeutic target and a possible predictive biomarker, particularly for READ. Future prospective and experimental studies on the expression of ARPC1B and immune cell infiltration in various cancer populations may enhance our understanding of tumor mechanisms and contribute to the development of techniques for targeted immunotherapy strategies.

Funding

Not applicable.

Ethics approval

The study from which we obtained our data was approved by the Hospital Ethics Review Committee of Yubei Hospital of Traditional Chinese Medicine (IRB no.: YBZYYLW2022-01).

Consent to participate

Informed consent was obtained from all individuals included in the study.

Consent to publication

All participants agreed to the terms of the informed consent form regarding publication of their data.

Data availability statement

CRediT authorship contribution statement

Chenxiong Zhang: Writing – review & editing, Writing – original draft, Software, Data curation, Conceptualization. **Hao Tan:** Writing – review & editing, Writing – original draft, Data curation. **Han Xu:** Writing – review & editing, Writing – original draft, Resources. **Jiaming Ding:** Resources, Data curation. **Huijuan Chen:** Writing – original draft, Visualization. **Xiaohong Liu:** Validation, Project administration. **Feng Sun:** Supervision, Methodology, Investigation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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