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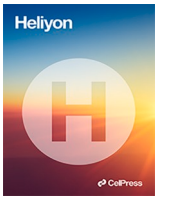

Research article

# Cordycepin enhances anti-tumor immunity in breast cancer by enhanceing ALB expression

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ABSTRACT

*Objective:* The treatment of breast cancer still faces great challenges, and it is necessary to continuously explore effective drugs and targets to promote immune precision medicine. This study aims to investigate the immune-related regulatory mechanism of cordycepin in breast cancer.

*Methods:* Network pharmacology was employed to discovery the action of cordyceps on breast cancer targets, molecular docking was employed to analyze the interaction pattern between core components and targets, and biological information analysis was used to explore the target-related immune mechanism and verified in vitro experiments.

*Results:* The results of this study indicate that cordycepin can effectively inhibit breast cancer. The roles of cordycepin's active component and its target gene ALB were elucidated through the combined use of network pharmacology and molecular docking. Bioinformatics analysis revealed convincing associations between ALB and many immune pathway marker genes. ALB was inhibited in tumor expression, and cordycepin was found to enhance the expression of ALB in vitro to play an anti-tumor role.

*Conclusion:* Cordycepin regulates immune suppression of tumor, which is expected to open a new chapter of breast cancer immunotherapy.

## 1. Introduction

The number of new cases of breast cancer (BRCA) worldwide reached 2.26 million in 2020, and it has officially replaced lung cancer as the first cancer in the world [1]. In recent years, thanks to the support of immunotherapy, the efficacy of BRCA has been significantly improved [2]. However, there is still a lot of room for improvement in the treatment [3]. The five-year survival rate of 90 % for BRCA does not equal the cure rate, and advanced breast cancer is almost incurable [4](5). At present, the treatment methods have reached the bottleneck, and it is urgent to find more effective therapies. Immunotherapy is an innovation in the field of cancer treatment [5]. As a moderately or weakly immunogenic tumor with low mutation burden, immunotherapy of breast cancer started

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late, but the exploration in recent years is in full bloom [6]. As a promising treatment, immunotherapy has brought new hope to breast cancer patients, especially those with triple-negative breast cancer [7]. In recent years, a series of clinical studies on immunotherapy drugs represented by immune checkpoint inhibitors have been carried out in the field of breast cancer treatment, and breakthroughs have been made [8]. More immunotherapy drugs have been approved and the accessibility of drugs has been improved.

The fruiting body of Cordyceps militaris (CM) holds significant importance as a reservoir of natural products with diverse biological activities. Widely recognized, it has been extensively employed both as a crude drug and a functional food in various Asian regions [9]. CM has been associated with a range of reported pharmacological activities, including antimicrobial, antifungal, antidiabetic, anti-inflammatory, antiaging, and neuroprotective properties [10]. In addition to the aforementioned activities, the extract from the fruiting body of Cordyceps militaris (CME) demonstrates anticancer effects against various cancer cell types, including ovarian, breast, lung, colon, and skin cancers [11](13). The principal active constituent of CME responsible for its anticancer activity is cordycepin, which is an analog of adenosine nucleoside [12]. While cordycepin demonstrates intriguing in vitro anticancer activity, its limited application in clinical settings is often attributed to a lack of specificity towards tumors. More investigation should be taken to find the mechanism behind cordycepin and BRCA.

This study is expected to provide an important theoretical basis for exploring the specific mechanism of cordycepin in the treatment of BRCA, and provide new ideas for related immunotherapy.

## 2. Materials and methods

### 2.1. Network pharmacology analysis and molecular docking

#### 2.1.1. Prediction of targets for cordycepin

First, search for the 2D and 3D structures of Cordycepin in the PubChem database (https://pubchem.ncbi.nlm.nih.gov/) [13], and download the corresponding SDF files containing both 2D and 3D structure information. Then, upload the 3D structure file of Cordycepin to the Pharm Mapper analysis platform (http://www.lilab-ecust.cn/pharmmapper/) to predict its 71 targets [14].

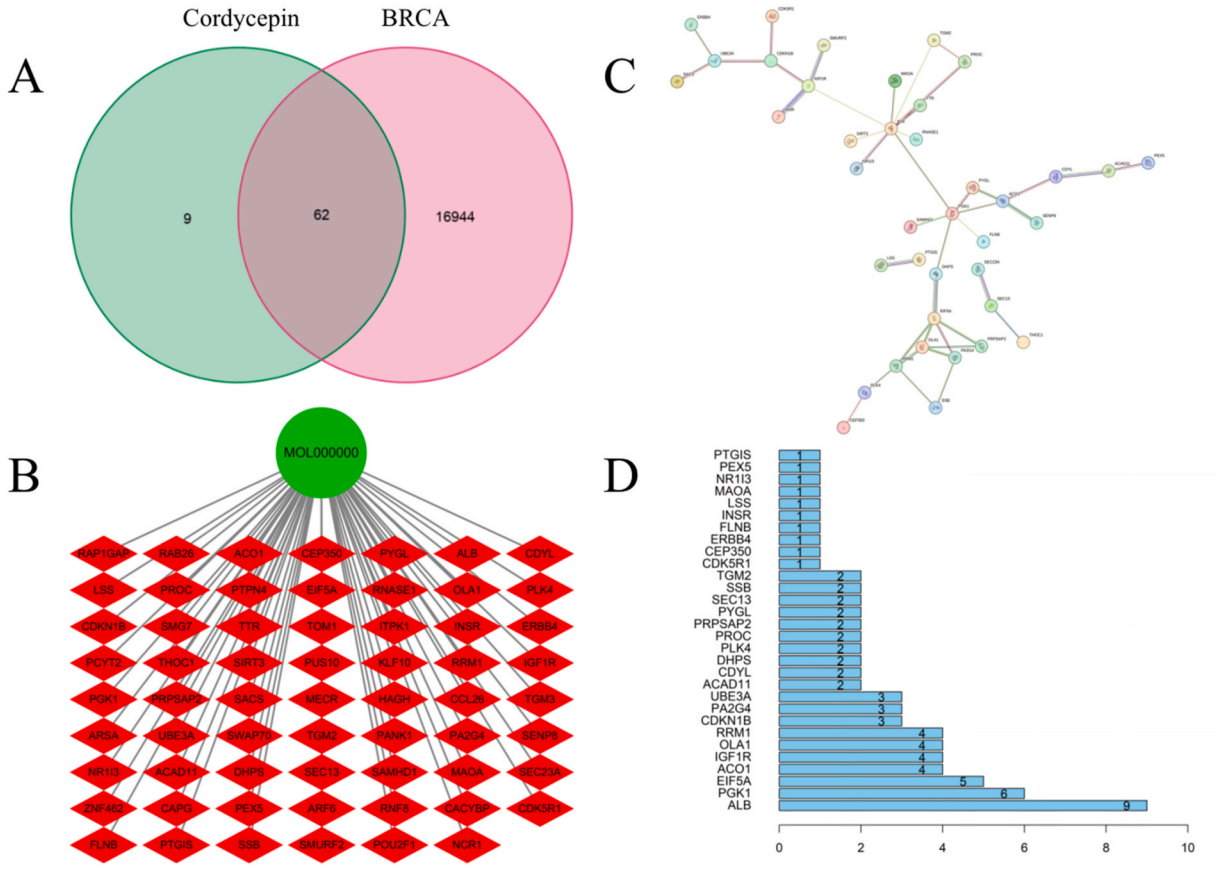


**Fig. 1.** Cordycepin Compounds- BRCA Targets.
The green circle was the active ingredient of cordycepin, and the red diamond was the target.
(A)Venn diagram of cordycepin targets and BRCA targets (B) PPI network of coincident Targets (C) The "Cordycepin Compounds- BRCA Targets" network (D) Quantification of adjacent nodes of the key targets.

#### 2.1.2. Target screening for BRCA

Using the keyword "Breast Cancer", search for disease-related targets in the GeneCards database (https://genealacart.genecards.org/) and OMIM database (https://www.omim.org/) [15](18). Take the results from both databases and take their union to obtain 17,006 BRCA-related targets.

#### 2.1.3. Construction of regulatory network for cordycepin in BRCA

Use Perl software to map Cordycepin targets and BRCA disease targets one-by-one, and obtain the intersection targets of Cordycepin and diseases. Then, use Cytoscape software (V3.7.1) to perform network visualization, obtaining a regulatory network of active ingredients-intersection targets (see Fig. 1). The types of nodes include active ingredients and targets.

#### 2.1.4. Construction of protein-protein interaction network (PPI) and core target screening for intersection targets

Take the intersection targets of Cordycepin and BRCA-related targets as the predicted targets of Cordycepin in BRCA treatment. Import the predicted targets into the STRING online website, restricting the study species to *Homo sapiens* and setting the others to default settings, to obtain a PPI network [16]. Draw a bar chart based on the number of neighboring nodes of the targets.

#### 2.1.5. Functional enrichment analysis

GO functional enrichment analysis mainly included three parts: biological process (BP), cellular component (CC) and molecular function (MF). The 62 intersection targets were processed using the Bioconductor bioinformatics package in R language software to obtain GO functional enrichment analysis and KEGG pathway enrichment analysis. Take $p < 0.05$ as statistically significant difference.

#### 2.1.6. Molecular docking

Molecular docking primarily served for the structural docking of small molecules to target proteins, enabling the evaluation of their binding affinity to specific binding sites [17]. A negative docking binding energy signifies the effective autonomous binding of the small molecule to the target protein. The general consensus is that the lower the energy of conformational stabilization during ligand binding to the receptor, the higher the likelihood of a significant effect. In this study, we performed molecular docking of cordycepin and ALB (PDB ID: 1N5U). The 3D structure map of hub targets was downloaded from Protein Data Bank (http://www.rcsb.org), saved in PDB format, and imported into AutoDock software for molecular docking [18]. PyMol software was used to visualize the docking results.

#### 2.1.7. Correlation analysis of ALB with immune pathway marker genes and immune cell infiltration

We obtained a standardized dataset from the University of California, Santa Cruz Genome Browser (UCSC) database (https://xenabrowser.net/) [19]. This dataset contained the expression data of the ALB gene and 150 marker genes related to five immune pathways, as well as 60 marker genes related to two immune checkpoint pathways in each sample. The expression values were then transformed using the log2 (x + 0.001) transformation. Subsequently, we computed the Pearson correlation between ALB and immune pathway marker genes. The Distribution of ALB expression across immune and molecular subtypes was analyzed from the TISIDB database (http://cis.hku.hk/TISIDB/browse.php) [20]. Moreover, we extracted tumor gene expression profiles and mapped them to GeneSymbol. Additionally, we employed the TIMER (https://cistrome.shinyapps.io/timer/) to ALB expression with immune infiltration level in different BRCA subtypes [21].

#### 2.1.8. Differential expression of ALB in breast cancer

From the TCGA database (https://portal.gdc.cancer.gov) to download and organize TCGA - BRCA (breast ductal carcinoma) project STAR process RNAseq data and extract the TPM format of the data, log2 (value + 1) handles the data.

#### 2.1.9. Cell culture and transient transfection

The human breast cancer cell lines MCF7 and MDA-MB-231, as well as the human monocyte cell line THP-1, were procured from BNCC. MCF7 and MDA-MB-231 cell lines were cultivated in DMEM F12 with 10 % FBS (Gibco, Thermo Fisher, USA), while the THP-1 cell line was cultured in RPMI medium 1640 with 10 % FBS (Gibco, Thermo Fisher, USA). Cultivation took place at 37 °C in a humidified environment with 5 % CO2. Co-culturing was facilitated using Transwell (Corning, USA).

#### 2.1.10. Drug

The cell lines (2 × 10^4 cells/well) were subjected to treatment with different concentrations of Cordycepin (10 μM, 20 μM, 50 μM, 100 μM, or 200 μM). Following an incubation period of 1 h, 12 h, and 24 h, the cells were washed twice with PBS. Subsequently, CCK-8 (0.5 mg/mL in PBS) was introduced to each well and incubated at 37 °C for 30 min.

#### 2.1.11. Quantitative reverse transcription-polymerase chain reaction (qRT-PCR)

Total RNA extraction was carried out using TRIzol reagent (Thermo Fisher, USA). Subsequently, quantitative reverse transcription-polymerase chain reaction (qRT-PCR) was conducted on the extracted RNA from each sample (2 μg) using FastStart Universal SYBR Green Master on a LightCycler 480 PCR System (Roche, USA). The cDNA served as a template with a reaction volume of 20 μl (2 μl of cDNA template, 10 μl of PCR mixture, 0.5 μl of forward and reverse primers, and an appropriate volume of water). The PCR reactions were conducted with the following cycling conditions: an initial DNA denaturation phase at 95 °C for 30 s, followed by 45 cycles at 94 °C for 15 s, 56 °C for 30 s, and 72 °C for 20 s. Each sample underwent three independent analyses. Using the 2-ΔΔCT method, data

from the threshold cycle (CT) were obtained and normalized to the levels of GAPDH in each sample. The mRNA expression levels were then compared to controls obtained from normal tissues. Below is a list of primer pair sequences for the targeted genes.

| Gene | Forward primer sequence (5′-3′) | Reverse primer sequence (5′-3′) |
|---|---|---|
| SOD1 | CTCACTCTCAGGAGACCATTGC | CCACAAGCCAAACGACTTCCAG |
| CAT | GTGCGGAGATTCAACACTGCCA | CGGCAATGTTCTCACACAGACG |
| GPX4 | ACAAGAACGGCTGCGTGGTGAA | GCCACACACTTGTGGAGCTAGA |
| PRDX6 | CAGCTACCACTGGCAGGAACTT | GGAAGGACCATCACACTATCCC |
| IL6 | AGACAGCCACTCACCTCTTCAG | TTCTGCCAGTGCCTCTTTGCTG |
| TNF | CTCTTCTGCCTGCTGCACTTTG | ATGGGCTACAGGCTTGTCACTC |
| IL10 | TCTCCGAGATGCCTTCAGCAGA | TCAGACAAGGCTTGGCAACCCA |
| IL4 | CCGTAACAGACATCTTTGCTGCC | GAGTGTCCTTCTCATGGTGGCT |
| CD86 | CCATCAGCTTGTCTGTTTCATTCC | GCTGTAATCCAAGGAATGTGGTC |
| NOS2 | GCTCTACACCTCCAATGTGACC | CTGCCGAGATTTGAGCCTCATG |
| CD206 | AGCCAACACCAGCTCCTCAAGA | CAAAACGCTCGCGCATTGTCCA |
| ARG1 | TCATCTGGGTGGATGCTCACAC | GAGAATCCTGGCACATCGGGAA |
| GAPDH | GTCTCCTCTGACTTCAACAGCG | ACCACCCTGTTGCTGTAGCCAA |

#### 2.1.12. ROS

In summary, cells were cultured in 6-well plates and treated as per experimental groups. Following medium removal, 10 μmol/L DCFH-DA (Beyotime, China) in 1 mL was added to each well, and incubation ensued for 20 min. Subsequently, cells were washed with serum-free medium to eliminate unabsorbed DCFH-DA. After sealing, fluorescence microscopy was employed to observe green color intensity (excitation wavelength: 485 nm, emission wavelength: 530 nm). ImageJ software analyzed the observed fluorescence to indicate cellular oxidation levels. Data were processed using GraphPad Prism 8.0 (version 8.0, GraphPad Software, La Jolla, CA, USA), and statistical significance was determined at $p < 0.05$.

#### 2.1.13. Cell culture and transient transfection

Human breast cancer cell lines MCF7 and MDA-MB-231 and human monocyte cell line THP-1 were purchased from BNCC. MCF7 and MDA-MB-231 cell lines were cultured in DMEM F12 with 10 % FBS (Gibco, Thermo Fisher, USA). THP-1 cell line was cultured in RPMI medium 1640 with 10 % FBS (Gibco, Thermo Fisher, USA). Cells were grown at 37 °C in a humidified environment containing 5 % CO2. Transwell (Corning, USA) was used to co-culture. The target sequences of small interfering RNA are listed.

| Taeget | target sequence (5′-3′) |
|---|---|
| si-ALB#1 | GTCCATTTGAAGATCATGTAAAA |
| si-ALB#2 | AAGATCATGTAAAATTAGTGAAT |

#### 2.1.14. 5-Ethynyl-2′-deoxyuridine (EdU) assay

EdU assay was performed using BeyoClick™ EdU Cell Proliferation Kit containing Alexa Fluor 594 (Boyetime, Shanghai, China). After rinsing with PBS, cells were incubated with EdU solution for 2 h and then stained with DAPI solution for nuclei. After washing, the samples were observed with an inverted microscope (Olympus).

## 3. Results

### 3.1. Construction of "Cordycepin Compounds- BRCA targets" network

A total of 62 overlapping targets were included after comparivng cordycepin targets and BRCA targets (Fig. 1A), and the cordycepin targets and BRCA targets were mapped one by one. The "Cordycepin Compounds- BRCA Targets" network was constructed, as the degree values of nodes were calculated in Cytoscape 3.7.2 (Fig. 1B).

### 3.2. Construction of a protein-protein interaction (PPI) network of targets

A PPI network was constructed after 62 targets were uploaded to the STRING database (Fig. 1C). According to the number of adjacent nodes of the key targets, *ALB, PGK1, EIF5A, ACO1, IGF1R, OLA1, RRM1, CDKN1B, PA2G4* and *UBE3A* were located in the core of the network, which might be the core genes of cordycepin against BRCA, and *ALB* was the most important one (Fig. 1D).

### 3.3. Analysis of GO pathway and KEGG pathway

GO functional enrichment analysis and KEGG pathway enrichment analysis were carried out using the Bioconductor bioinformatics package in R language software. With $p < 0.05$ as the screening condition, in GO functional enrichment analysis, the top three biological processes that were significantly enriched by BP included: protein tetramerization, regulation of protein complex disassembly

and somatic diversification of immunoglobulins. The top three cellular components that were significantly enriched by CC included: secretory granule lumen, cytoplasmic vesicle lumen, and vesicle lumen. The top 10 molecular functions with obvious MF enrichment included: core promoter sequence-specific DNA binding, insulin receptor substrate binding, and insulin-like growth factor I binding (Fig. 2A–B). In KEGG pathway enrichment analysis, the top three pathways are protein tetramerization, regulation of protein complex disassembly, and somatic diversification of immunoglobulins (Fig. 2C–D).

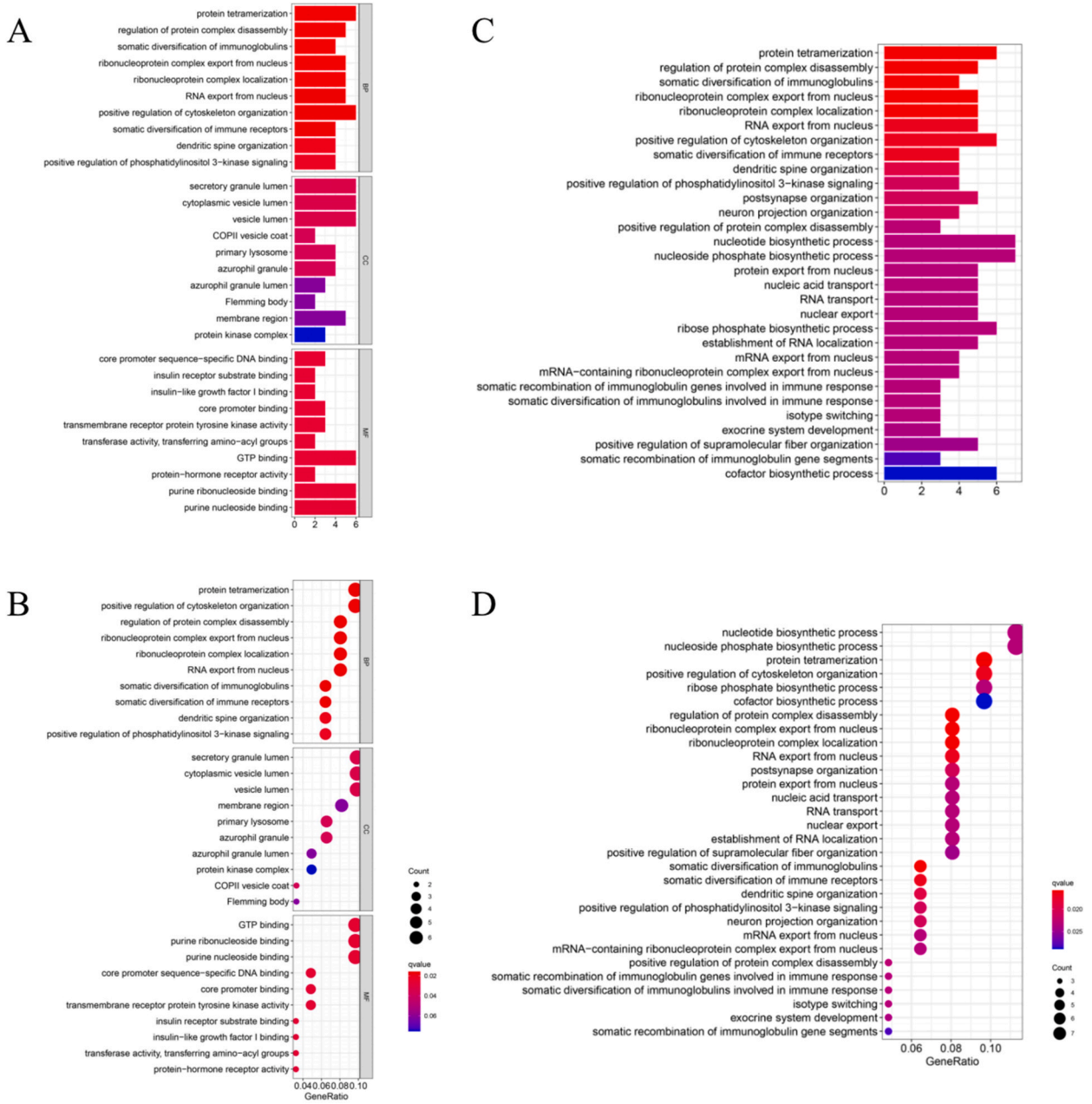


**Fig. 2.** Diagram for GO and KEGG enrichment analysis.
The bubble size represents the number of enriched genes, and the bubble color difference represents the significant magnitude of target gene enrichment.
(A)Molecular Function enrichment analysis (B)Cellular Component enrichment analysis (C) Biological Process enrichment analysis (D) KEGG functional enrichment analysis.

### 3.4. Molecular docking of the binding interaction between cordycepin and ALB

Through network pharmacology analysis and molecular docking, we discovered that cordycepin can bind to ALB through hydrogen bonding and strong electrostatic interactions, indicating a highly stable binding (Fig. 3A–B). The molecular formula of cordycepin was shown in Fig. 3C.

### 3.5. ALB with immune pathway marker genes and immune cell infiltration in different BRCA subtypes

Subsequently, we performed bioinformatics analysis to investigate the regulatory effects of ALB on immune modulatory genes and immune infiltration in different BRCA subtypes, and its expression is relatively low in tumors (Fig. 4A–C). ALB showed a significant association with immune infiltration scores of B cells in BRCA, $CD8^+$ T cells in BRCA-Luminal (Fig. 4D). Furthermore, The results revealed significant correlations between ALB and multiple immune pathway markers (Fig. 4E).

Analysis of the infiltration scores of B cells, $CD8^+$ T cells, $CD4^+$ T cell, macrophages, neutrophils, and dendritic cells based on the expression levels of ALB in patients. (B) Associations between ALB expression and immune subtypes across breast cancer. (C) Associations between ALB expression and molecular subtypes across breast cancer. (D) A comparison was performed between the ALB gene and 60 genes associated with two categories of immune checkpoint pathways to assess their correlation. * represents $p < 0.05$, ** represents $p < 0.001$, *** represents $p < 0.0001$.

### 3.6. Cordycepin is effective in treating human breast cancer cell lines in vitro

We performed experimental treatment of human breast cancer cell lines MCF7 and MDA-MB-231 in vitro with five concentrations of cordycepin, 10 μM, 20 μM, 50 μM, 100 μM or 200 μM. The viability of human breast cancer cell lines decreased rapidly with

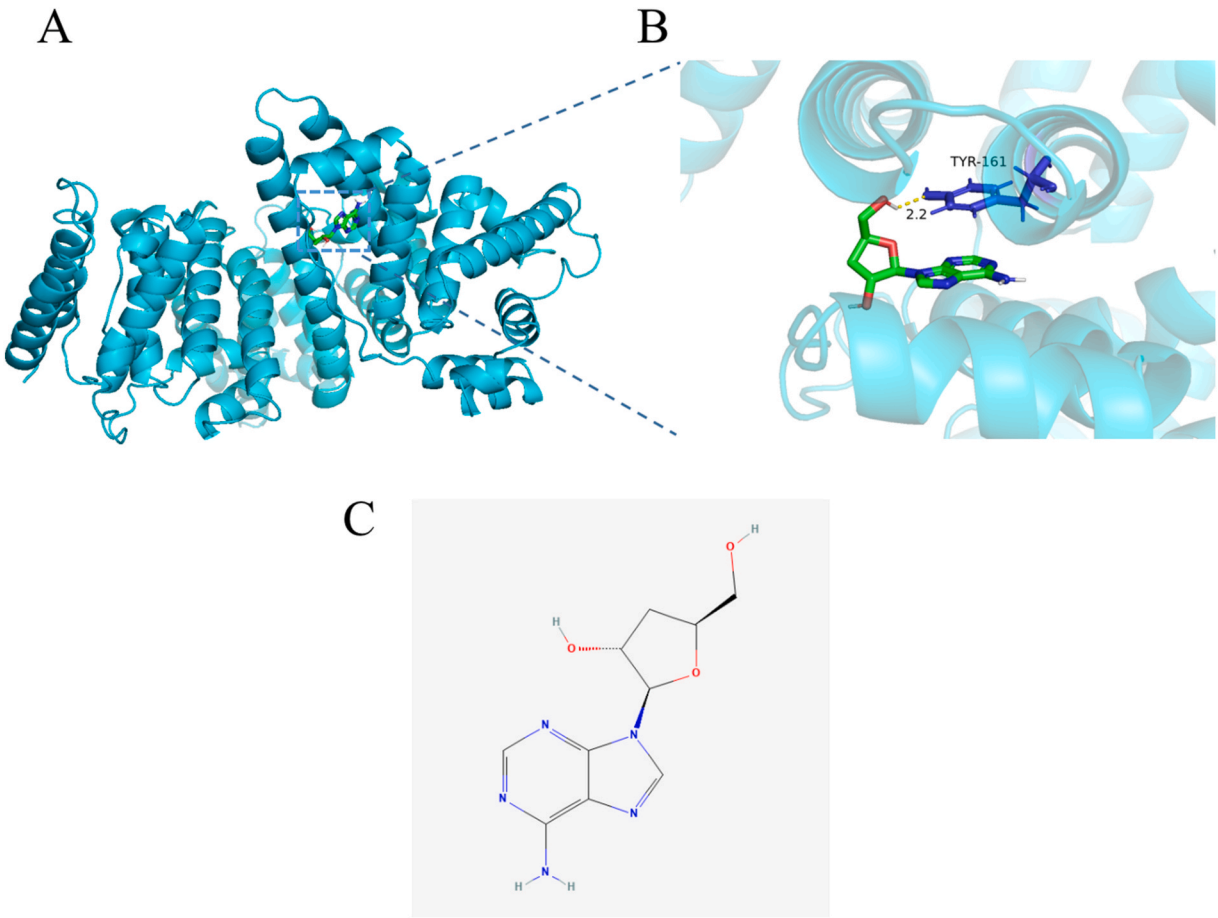


**Fig. 3.** Molecular docking of the binding interaction between cordycepin and ALB.
(A,B) The molecular docking of cordycepin and ALB, where the blue box portion is magnified, shows the interaction of additional residues and hydrogen bonds. The blue structure indicates the binding site of ALB protein to cordycepin, the yellow hydrogen bond, and the bond energy is labeled next to it. (C) Chemical structure diagram of cordycepin.

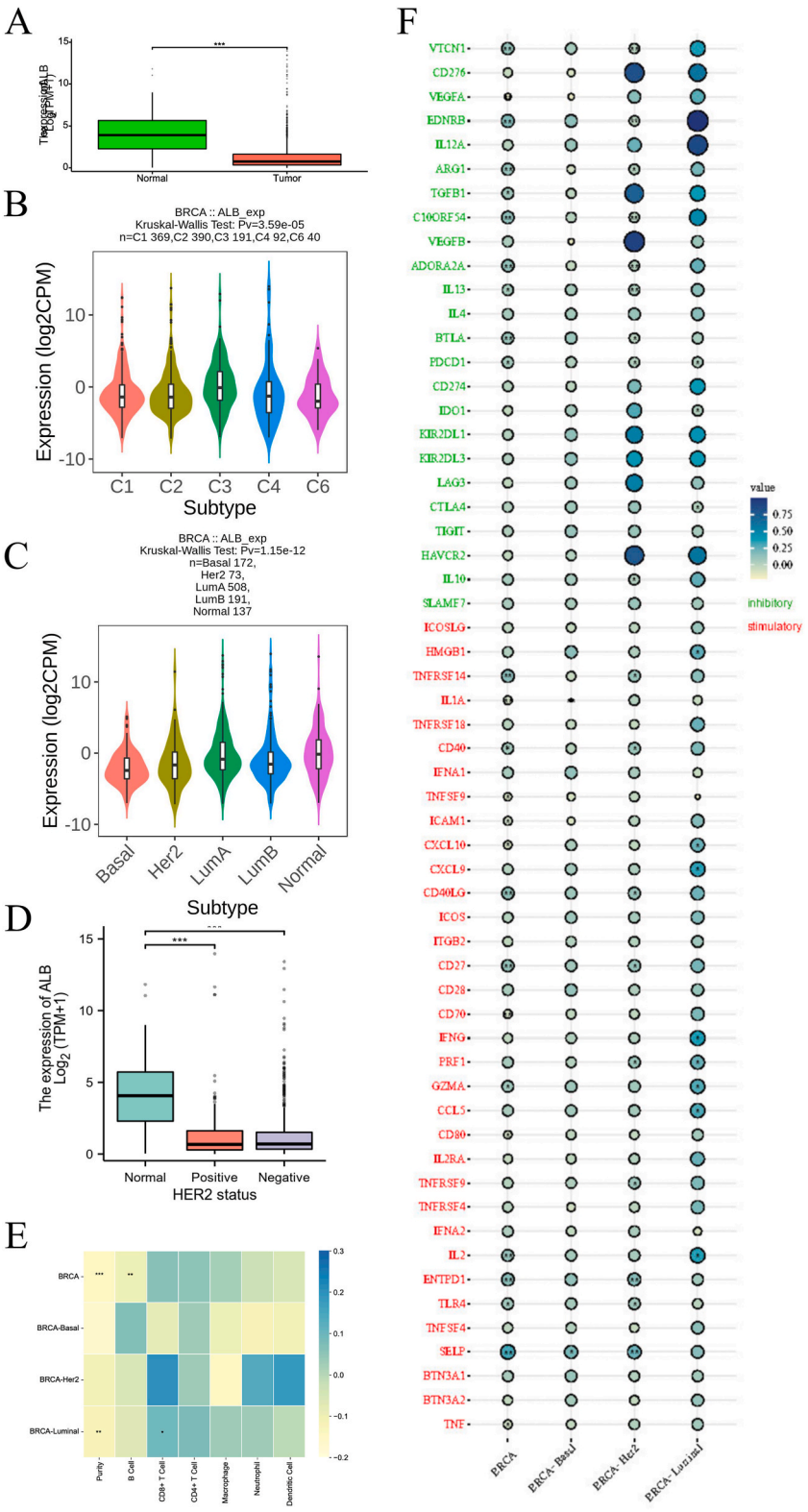


**Fig. 4.** The regulatory effects of the ALB gene on immune modulatory genes and immune infiltration in different BRCA subtypes.

increasing concentrations of cordycepin, but the three therapeutic concentrations of 50 μM, 100 μM or 200 μM had the same inhibitory ability for human breast cancer cell lines (Fig. 5A–B). We then examined changes in the transcript levels of ALB in human breast cancer cell lines after cordycepin treatment. In contrast to the tendency of rapid decrease in cell viability, the transcript levels of ALB in human breast cancer cell lines increased rapidly after cordycepin treatment until 50 μM after which there was no further change (Fig. 5C–D). For this reason, we selected 50 μM cordycepin as the therapeutic concentration in vitro. Elevated reactive oxygen species (ROS) lead to

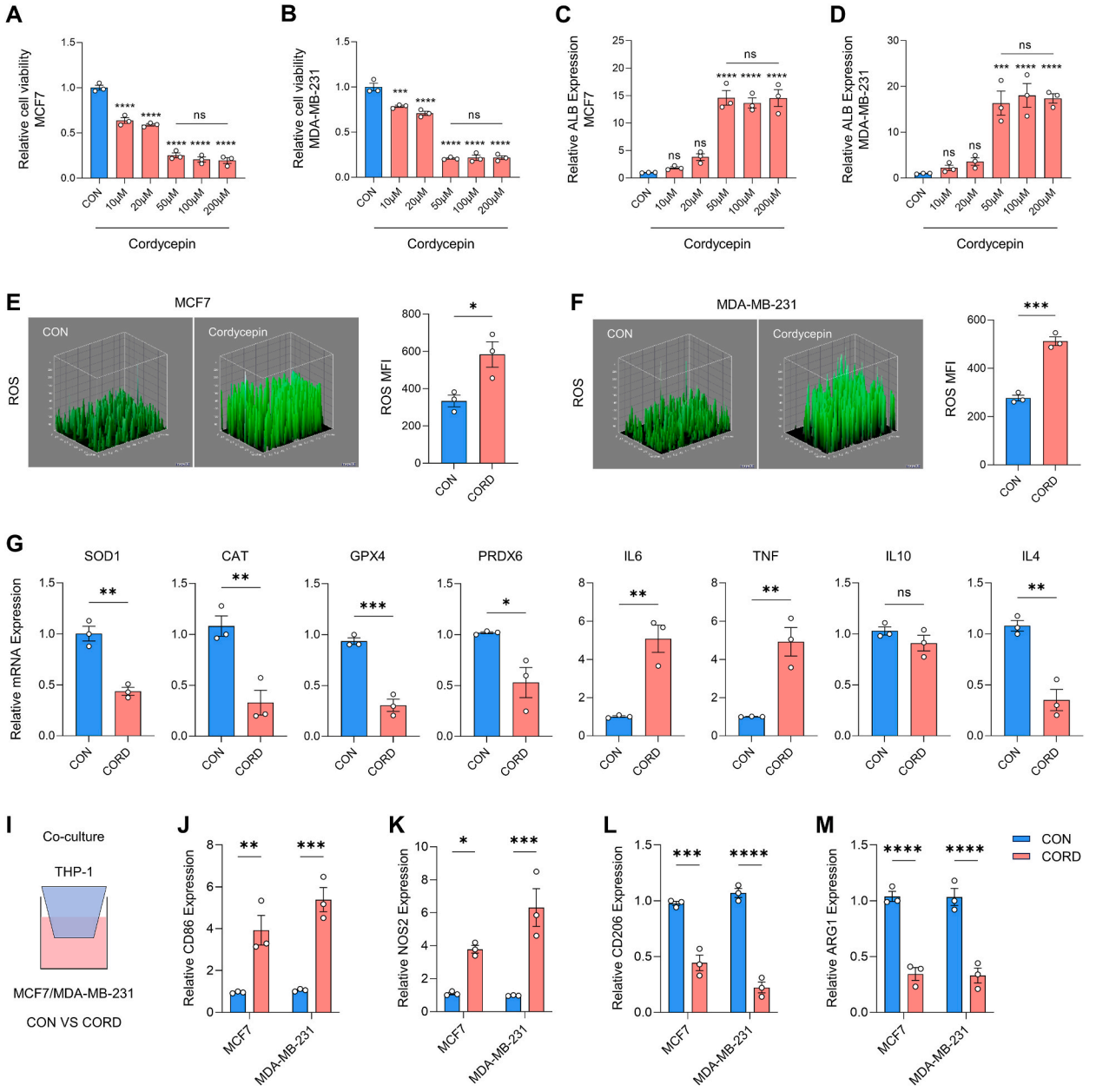


**Fig. 5.** Cordycepin is effective in treating human breast cancer cell lines in vitro.
(A–B) Changes in cell viability of MCF7 and MDA-MB-231 cell lines after treatment with different concentrations of cordycepin and relative quantitative analysis. (C–D) Transcriptional alterations of ALB in MCF7 and MDA-MB-231 cell lines after treatment with different concentrations of cordycepin and relative quantitative analysis. (E–F) Changes in ROS intensity in MCF7 and MDA-MB-231 cell lines after cordycepin treatment and quantitative analysis of mean fluorescence intensity. (G) Transcriptional changes of inflammatory cytokines in cordycepin-treated human breast cancer cell lines with relative quantitative analysis. (I) Schematic representation of human breast cancer cell lines co-cultured with THP-1 cell line before and after cordycepin treatment. (J–M) Changes in transcript levels of M1/M2 makers in THP-1 cell lines co-cultured with human breast cancer cell lines before and after cordycepin treatment. n = 3. * < 0.05, **< 0.01, ***< 0.001, ****< 0.0001. The results are presented as mean ± SEM.

apoptosis, and for this reason we examined the levels of ROS in human breast cancer cell lines after cordycepin treatment. We observed a rapid increase in ROS levels in cordycepin-treated human breast cancer cell lines, suggesting that a response to cordycepin treatment exists in human breast cancer cell lines (Fig. 5E–F). Given this finding, we examined the activity of ROS clearance enzymes in human breast cancer cell lines before and after cordycepin treatment. Transcript levels of SOD1, CAT, GPX4, and PRDX6 decreased rapidly after cordycepin treatment, indicating a rapid decrease in ROS scavenging capacity in human breast cancer cell lines after cordycepin treatment. Meanwhile elevated ROS levels in human breast cancer cell lines were also accompanied by elevated transcription of pro-inflammatory cytokines, such as IL6 and TNF. At the same time, the transcription of anti-inflammatory cytokines, such as IL4 and IL10, was significantly decreased (Fig. 5G). Macrophage polarization may have a different role for tumor progression, and for this reason we examined the phenotype of THP-1 cells after co-culture of human breast cancer cell lines before and after treatment with cordycepin.

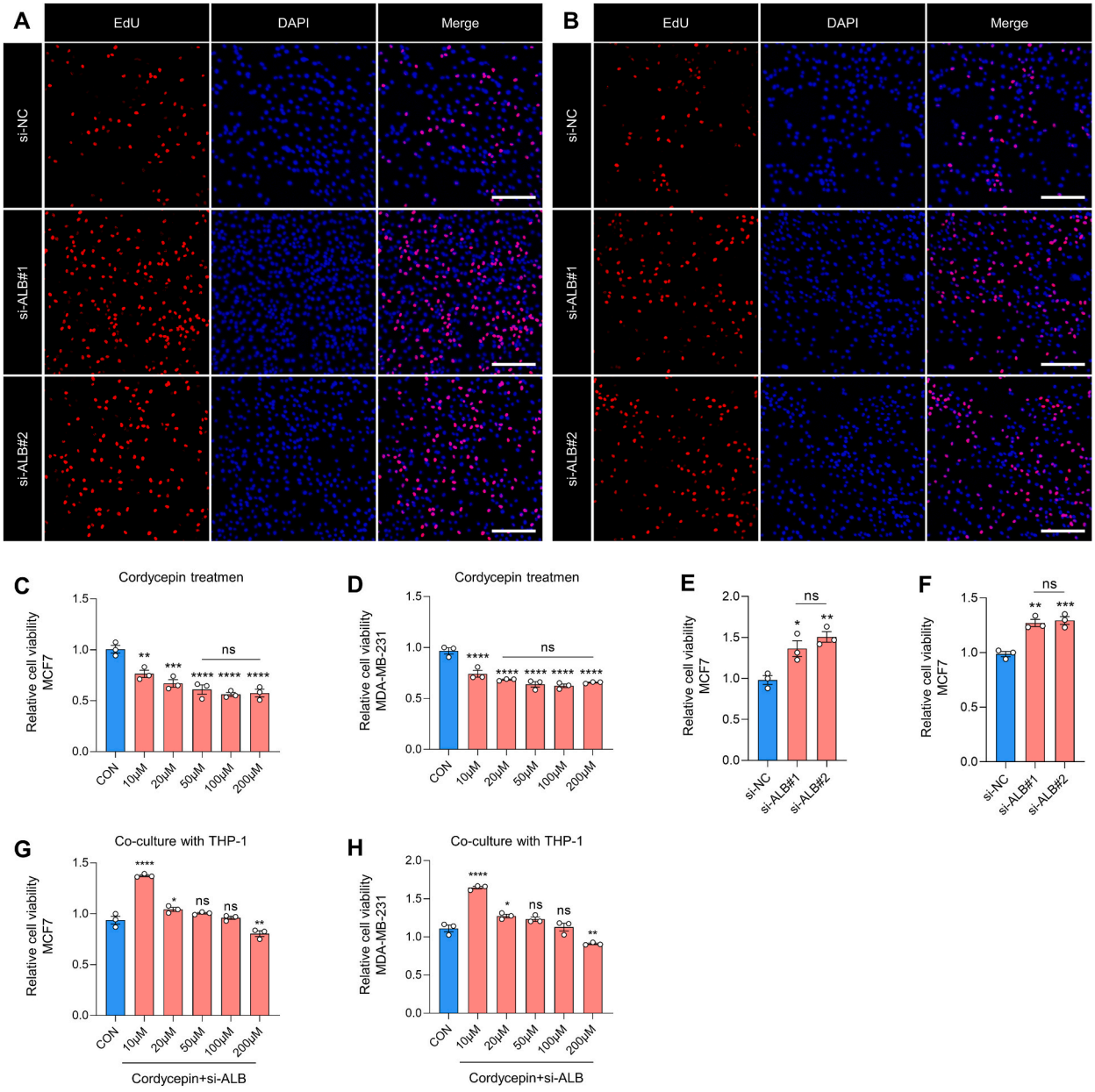


**Fig. 6.** ALB inhibits the proliferative capacity of breast cancer cell lines. (A–B) Representative EdU staining results of MCF-7 and MDA-MB-231 cell lines before and after ALB inhibition. (C–D) CCK8 results of MCF-7 and MDA-MB-231 cell lines before and after cordycepin treatment and relative quantitative analysis. (E–F) CCK8 results of MCF-7 and MDA-MB-231 cell lines co-cultured with cordycepin-treated THP-1 before and after inhibition of ALB and analyzed for relative quantification. (G–H) CCK8 results of MCF-7 and MDA-MB-231 cell lines before and after ALB inhibition and relative quantitative analysis.

Upon co-culture with cordycepin-treated human breast cancer cell lines, the transcription of CD86 and NOS2 in THP-1 was enhanced, reflecting the tendency of M1 polarization. Meanwhile, the transcription of CD206 and ARG1 in THP-1 was significantly inhibited, exhibiting suppression of M2 polarization (Fig. 5I–M). Firstly, we observed the effect of cordycepin in direct treatment of breast cancer cell lines.The results of CCK8 suggested that cordycepin had a slight inhibitory effect on MCF7 and MDA-MB-231, but not as significant as co-culture with THP-1 (Fig. 6 C-D). To clarify the effect of ALB on breast cancer cell lines, we used small interfering RNA to inhibit ALB expression in breast cancer cell lines. The results of EdU staining suggested that the proliferative capacity of MCF7 and MDA-MB-231 cell lines was significantly increased after ALB knockdown, which was similarly corroborated by the results of CCK8 (Fig. 6 E-F). THP-1 after cordycepin stimulation no longer exhibits strong inhibitory effects on breast cancer cell lines with knocked-down ALB (Fig. 6).

## 4. Discussion

At present, the research on the anticancer effect of cordycepin has progressed rapidly, and more and more mechanisms have been discovered [22]. Cordycepin possesses a number of pharmacological functions including anti-cancer effect, anti-inflammatory and neuroprotective effects [23](27). However, its detailed anticancer mechanisms in breast cancer are still not clear.

Cordycepin can play the role of bidirectional immune regulation by improving cellular immune function, inhibiting the production of IL-2 by plant hemagglutinins and the expansion of monocytes in peripheral blood [24]. Anti-il-10 neutral antibody could not completely block the inhibitory effect of cordycepin on IL-2 production. Under the action of cordycepin, mature dendritic cells can induce the proliferation of regulatory T cells, inhibit cell division, promote cell differentiation, change the structure and distribution of substances on the cell membrane, and promote the transformation of T lymphocytes [25]. It can also improve the phagocytic function of the body's monocyte-macrophage system, activate macrophages to produce cytotoxins and directly kill cancer cells. Cordycepin resulted in enhanced transcription of CD86 and NOS2 in THP-1 cells, reflecting the trend towards M1 polarization. At the same time, the transcription of CD206 and ARG1 in THP-1 cells was significantly inhibited, which was manifested as the inhibition of M2 polarization. Human total ALB pool is affected by ALB gene expression and ALB catabolism [26]. The gene ALB has previously been observed to contribute to the metabolic reprogramming of HCC(31). In different pathophysiological states, ALB can stimulate or alleviate immune cell activation [27]. The main way is to stimulate the intrinsic immune cells such as neutrophils, macrophages and vascular endothelial cells through specific receptors to induce various inflammatory mediators, including cytokines, arachidonic acids, prostaglandins, thromboxins, leukotrienes and various ROS and RNS substances [28](34). Its expression is low in breast tumors and stable and consistent in different subtypes and different periods, suggesting that it may be a potential therapeutic target.

Although cordycepin has shown promising experimental results in inhibiting breast cancer, there are still many challenges. The high production cost of cordycepin makes it relatively expensive, limiting its wide clinical use. There are still many ways to go in the clinical application of Chinese medicine. In the clinical application of Chinese medicine, it is necessary to strengthen the quality control, in-depth study of its pharmacological mechanism, establish a scientific evaluation system, and combine clinical practice experience to select and apply Chinese medicine reasonably. The efficacy of single drug is limited, and drugs with multiple mechanisms of action are urgently needed to improve the efficacy, including immune combined with chemotherapy, dual immune combination, and immune combined with targeted therapy. How to explore the best combination regimen and find biomarkers of benefit are still unclear. How to further improve the efficacy of immunotherapy is the key to its clinical application in the future. In clinical application, it is necessary to weigh its advantages and disadvantages, and make reasonable decisions based on specific conditions and patient conditions. Cordycepin regulates immune suppression of tumor, which is expected to open a new chapter of breast cancer immunotherapy.

Cordycepin, as a natural source of anti-tumor active ingredient, Safety is high. Our finding that cordycepin can enhance anti-tumor immunity in breast cancer by enhanceing ALB expressio This may provide a theoretical basis for the application of cordycepin derivatives in the treatment of breast cancer. Cordycepin can be used as an adjuvant drug to improve the efficacy of anti-tumor drugs, which provides new ideas and theoretical basis for the development of anticancer drugs in the future.

*Consent for publication*

All the authors provided written informed consent for the publication of the manuscript.

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*Availability of data and material*

Cordycepin related data are available in the public repository.

*Contributors*

All contributors are listed as authors.

## CRediT authorship contribution statement

**Lin Chen:** Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Formal analysis, Data curation, Conceptualization. **Weihao Wei:** Writing – original draft, Visualization, Validation, Data curation, Conceptualization. **Jin Sun:** Writing – original draft, Validation, Supervision, Software, Methodology, Conceptualization. **Beicheng Sun:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Rong Deng:** Writing – review & editing, Visualization, Validation, Supervision, Conceptualization.

## 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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