Observational Study

Medicine

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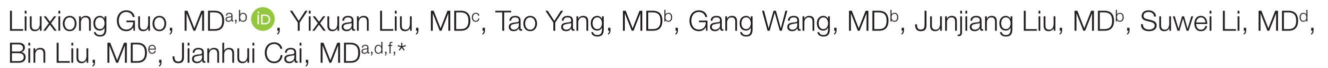
CAV1 and KRT5 are potential targets for prostate cancer



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Abstract

Prostate cancer is the most common malignant tumor of male urogenital system that occurs in prostate epithelium. However, relationship between CAV1 and KRT5 and prostate cancer remains unclear. The prostate cancer datasets GSE114740 and GSE200879 were downloaded from Gene Expression Omnibus generated by GPL11154 and GPL32170. De-batch processing was performed, differentially expressed genes (DEGs) were screened, and weighted gene co-expression network analysis. The construction and analysis of protein–protein interaction network, functional enrichment analysis, gene set enrichment analysis. Gene expression heat map was drawn and immune infiltration analysis was performed. Comparative toxicogenomics database analysis were performed to find the disease most related to core gene. In addition, the cell experiment was performed to verify the role of CAV1 and KRT5 by western blot. Divided into 4 groups: control, prostate cancer, prostate cancer-over expression, and prostate cancer- knock out. TargetScan screened miRNAs that regulated central DEGs; 770 DEGs were identified. According to Gene Ontology analysis, they were mainly concentrated in actin binding and G protein coupled receptor binding. In Kyoto Encyclopedia of Gene and Genome analysis, they were mainly concentrated in PI3K-Akt signal pathway, MAPK signal pathway, and ErbB signal pathway. The intersection of enrichment terms of differentially expressed genes and GOKEGG enrichment terms was mainly concentrated in ErbB signaling pathway and MAPK signaling pathway. Three important modules were generated. The protein–protein interaction network obtained 8 core genes (CAV1, BDNF, TGFB3, FGFR1, PRKCA, DLG4, SNAI2, KRT5). Heat map of gene expression showed that core genes (CAV1, TGFB3, FGFR1, SNAI2, KRT5) are highly expressed in prostate cancer tissues and low in normal tissues. Comparative toxicogenomics database analysis showed that core genes (CAV1, TGFB3, FGFR1, SNAI2, KRT5) were associated with prostate tumor, cancer, tumor metastasis, necrosis, and inflammation. CAV1 and KRT5 are up-regulated in prostate cancer. CAV1 and KRT5 are highly expressed in prostate cancer. The higher expression of CAV1 and KRT5, the worse prognosis.

Abbreviations: CTD = comparative toxicogenomics database, DEGs = differential epigenetic genes, GO = Gene Ontology, GSEA = gene set enrichment analysis, KEGG = Kyoto Encyclopedia of Gene and Genome, KO = knock out, OE = over expression, PPI = protein–protein interaction, STRING = Search Tool for the Retrieval of Interacting Genes, WGCNA = Weighted Gene Co-Expression Network Analysis.

Keywords: CAV1, KRT5, prostate cancer, targets

1. Introduction

Prostate cancer is a tumor caused by malignant proliferation of the epithelial cells of the prostate. Prostate cancer is associated with country's development index, which is more common in developed countries.[1] In general, prostate cancer has the lowest morbidity and mortality in Asia, while Western Europe, Australia and North America have relatively high morbidity but low mortality.[2] According to GLOBOCAN 2020 data, 7.3% of new cancer cases and 3.8% of deaths in 2020 were attributed to prostate cancer.[3] It is reported that in 2020, there were 1,414,000 new cancer cases worldwide and 375,304 cancer patients died. The global incidence of prostate cancer is 30.7 per 100,000 people, and the global mortality rate is 7.7 per 100,000 people.[4] The prostate is located at the base of the pelvis and

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

This study was approved by the Ethics Committee of Hebei General Hospital.

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How to cite this article: Guo L, Liu Y, Yang T, Wang G, Liu J, Li S, Liu B, Cai J. CAV1 and KRT5 are potential targets for prostate cancer. Medicine 2023;102:49(e36473).

Received: 16 October 2023 / Received in final form: 13 November 2023 / Accepted: 14 November 2023

http://dx.doi.org/10.1097/MD.0000000000036473

penis, and the tissue is mainly glandular. Malignant tumors caused by glands are classified as cancer, which is the most common prostate cancer, accounting for more than 95%.[5] Prostate cancer is usually slow-growing, often asymptomatic in the early stage, and it will produce corresponding clinical manifestations with the development of the tumor. Gradually enlarged prostate gland oppresses urethra can cause progressive dysuria, tumor oppresses rectum can cause defecation difficulty or intestinal obstruction, can also oppress vas deferens to cause ejaculation deficiency, oppress nerve to cause perineal pain, and can radiate to sciatic nerve. Prostate cancer is usually diagnosed by digital rectal examination and blood testing for prostate-specific antigen. Definitive diagnosis usually requires a biopsy of prostate tissue.[6] Treatment depends on the severity of the disease and the overall health of the patient and includes observation (for low-risk patients), surgical resection, radiotherapy, hormonal therapy, and chemotherapy.[7] The exact cause of prostate cancer is unclear, but the DNA mutation that leads to mutations or abnormal gene fusion may be an event. Advanced age, family history of prostate cancer (especially BRCA1 and BRCA2 gene mutations), Lynch syndrome, obesity, unhealthy diet, alcohol consumption, smoking and specific drugs are known risk factors, and there is growing evidence that they contribute to potential causes.[8–10]

Caveolin-1 (Cav1) gene is located on chromosome 7 and is responsible for encoding the Caveolin-1 (CAV-1) protein, a 22 kDa integral membrane protein.[11] The CAV-1 protein consists of 178 amino acids and exists in 2 isoforms, namely CAV-1α and CAV-1β. Caveolin-1 plays a crucial role in the formation of caveolae and is involved in various physiological and pathological processes, including cell signal transduction, lipid transport, and the regulation of cell growth.[12] KRT5 is a gene located on chromosome 12, and the protein encoded by this gene is a member of the keratin gene family.[13] Mutations or abnormalities in the KRT5 gene can lead to various skin disorders, as keratins are crucial for maintaining the structural integrity of epithelial tissues.

As an important part of the development of life science, bioinformatics has been at the forefront of life science and technology research. In recent years, China's biotechnology has developed by leaps and bounds, and bioinformation resources have also grown explosively. Bioinformatics reveals the biological significance represented by big data, which is a bridge between data and clinic. Represented by the analysis and reporting of gene detection data, bioinformatics plays an important role in tumor treatment.[14,15]

However, relationship between CAV1, KRT5 and prostate cancer is not clear. Therefore, the study intends to use bioinformatics technology to mine core genes between prostate cancer and normal tissue, and carry out analysis. The public dataset was used to verify significant role of CAV1 and KRT5 in prostate cancer. And it was verified by basic cell experiment.

2. Method

2.1. Prostate cancer data set

The prostate cancer dataset GSE114740 and GSE200879 were downloaded from Gene Expression Omnibus generated by GPL11154 and GPL32170. GSE114740[16] includes 10 prostate cancer and 10 normal tissue samples. GSE200879 includes 128 prostate cancer and 9 normal tissue samples.

2.2. De-batch processing

R software package was used to merge datasets GSE114740 and GSE200879. For merging of multiple data sets, R software package was used in Silico Mergingto merge the data sets to get the merge matrix. R software package limma removes batch effect. Clean up possible missing values, outliers, etc. Data normalization or normalization was performed to ensure that the data were on the same scale. Exploratory data analyses of batch effects were performed. The matrix batch effect after removal was obtained.

2.3. Screening of differentially expressed genes (DEGs)

Screening of differentially expressed genes is a critical step in gene expression analysis, helping to identify genes whose expression levels change significantly between conditions. Probe aggregation and background correction of merge matrix of GSE114740 and GSE200879 using R package "limma." *P* value were adjusted using Benjamini-Hochberg method. The multiple change (FC) is calculated using error detection rate (FDR). The cutoff value of DEG is $P < .05$ and FC is >1.5. And make a visual representation of the volcano.

2.4. Weighted Gene Co-expression Network Analysis (WGCNA)

WGCNA is a systems biology method for discovering gene co-expression modules and exploring relationships between genes. Gene networks were constructed to identify modules associated with biological features or disease states. Using de-batch and post-merge matrix of GSE114740 and GSE200879 to calculate median absolute deviation of each gene. The good samples genes method of R package WGCNA was used to remove the outlier genes and samples, construct scale-free co-expression network. We calculated the characteristic gene differences of the modules, and selected tangent line for module tree view, incorporated part of modules. Grey module is considered as a set of genes that could not be assigned to any module. Visualize co-expression modules, analyze the properties of modules, identify marker genes, and understand their relationship to biological features.

2.5. Protein–protein interaction (PPI) network

Protein–protein Interaction (PPI) network is a network composed of protein interactions, which reveals the interaction pattern of proteins in cells and helps to understand intracellular signal transduction, metabolic pathways, cell cycle and other biological processes. Search Tool for the Retrieval of Interacting Genes (STRING) is a search system for known and predicted PPI. STRING database also contains the predicted results using bioinformatics methods. The differential genes were input into STRING to construct PPI network and predict the core genes. PPI network was visualized, core genes are predicted by Cytoscape software. First of all, we import PPI network into the Cytoscape, and then genes with best correlation were calculated by MCC and MNC. Finally, core genes was obtained after visualization.

2.6. Functional enrichment analysis

Functional enrichment analysis is a method used to understand collections of genes or proteins in high-throughput biological data, which can help reveal the association of these collections with specific biological processes, cellular components, or molecular functions. Gene Ontology (GO) Analysis and Kyoto Encyclopedia of Gene and Genome (KEGG) analysis are computational methods for evaluating function and biological pathways of genetics. The list of differential genes screened by Wayne map was input into KEGG rest API obtained latest KEGG Pathway gene annotation, which was used as background. Gene set enrichment results were obtained using R package cluster Profiler.

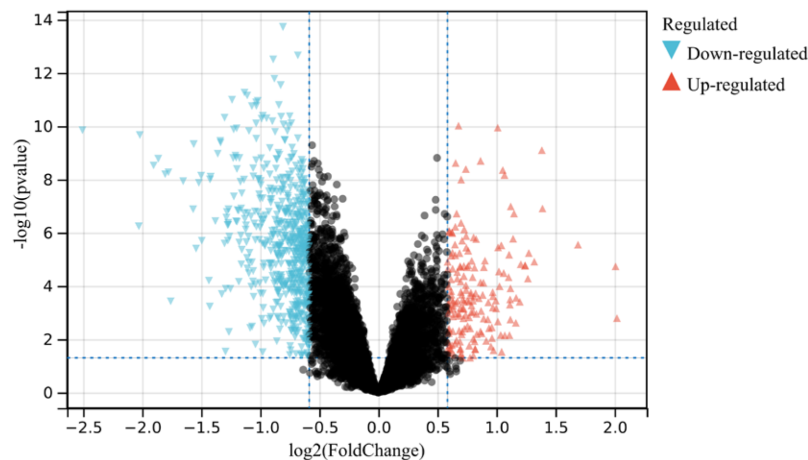

Figure 1. Analysis of differentially expressed genes. 770 DEGs were identified. DEGs = differentially expressed genes.

Metascape (http://metascape.org/) is a powerful gene function annotation and analysis tool that can realize cognition of gene or protein function, and can be visually exported. We used Metascape to analyze functional enrichment of above differential gene list and derive it.

2.7. Gene set enrichment analysis (GSEA)

GSEA is a systems biology approach used to determine whether genes in a given gene set are enriched in some biological process, pathway, or function, capable of providing insight into the biological implications of the gene set of interest under study. GSEA is based on level-specific gene probes that evaluate data from microarrays and is a way to uncover genomic expression data through fundamental knowledge. Samples were divided into 2 groups: prostate cancer and normal tissue. Relevant pathways and molecular mechanisms were evaluated. 5 is minimum gene set and 5000 is maximum gene set, and 1000 resampling times. The whole genome was analyzed by GO and KEGG.

2.8. Gene expression heat map

Gene expression heat map is a graphical representation method used to visualize gene expression data to identify gene expression patterns under different biological conditions. Gene expression heat map is a commonly used tool in systems biology and bioinformatics research to help understand the regulation and interrelationship of genes in different biological processes. The expression of core genes in GSE114740 and GSE200879 PPI networks was mapped using the R-packet heat map, and to visualize difference of core gene expression between prostatic cancer and normal samples.

2.9. Immune infiltration analysis

Immune infiltration analysis is a method used to study the infiltration of immune cells in biological samples, which helps to understand the role of the immune system in the development and treatment of diseases, especially in diseases such as cancer. CIBERSORT (http://CIBERSORT.stanford.edu/) is a very common method for calculating immune cell infiltration. We applied the integrated bioinformatics method and used the CIBERSORT software package to analyze the de-batch merging matrix of GSE114740 and GSE200879. The immune cell subtype expression matrix was deconvolvated using linear support vector regression principle to estimate immune cell abundance. At the same time, the samples with sufficient confidence were selected by using confidence $P < .05$as the truncation criterion.

2.10. Comparative toxicogenomics database (CTD) analysis

CTD provides manually curated information on chemo-gene/protein interactions, gene-disease relationships, is a powerful public database. The core genes were input into CTD, so as to find the diseases most related to the core gene, and Excel was used to draw radar map of differential expression of each gene.

2.11. Western blotting

Western blotting, also known as immunoblotting, is a method to detect the expression of a certain protein in complex samples according to the specific binding of antigens and antibodies, and can qualitatively and semi-quantitatively analyze proteins.

2.11.1. Protein extraction. Proteins are extracted using an appropriate lysis buffer to ensure complete disruption of cell membranes and release of proteins.

2.11.2. Electrophoresis separation. The extracted protein samples are separated through Sodium Dodecyl Sulfate Polyacrylamide Gel Electrophoresis (SDS-PAGE), which separates proteins based on their molecular weight.

2.11.3. Membrane transfer. Separated proteins are transferred from the gel to a solid membrane, such as nitrocellulose or polyvinylidene difluoride (PVDF), through methods like electroblotting or capillary transfer.

2.11.4. Blocking. A blocking solution, typically containing bovine serum albumin (BSA) or nonfat dry milk, is applied to the membrane to prevent nonspecific binding.

2.11.5. Primary antibody incubation. A specific primary antibody, targeting the protein of interest, is applied to the membrane, binding specifically to the target protein.

2.11.6. Washing. Unbound primary antibody is removed through washing, reducing nonspecific binding.

2.11.7. Secondary antibody incubation. A specific secondary antibody, conjugated with a marker such as an enzyme or fluorescent dye, is applied to the membrane, binding to the primary antibody.

2.11.8. Washing. Unbound secondary antibody is washed away through additional washing steps.

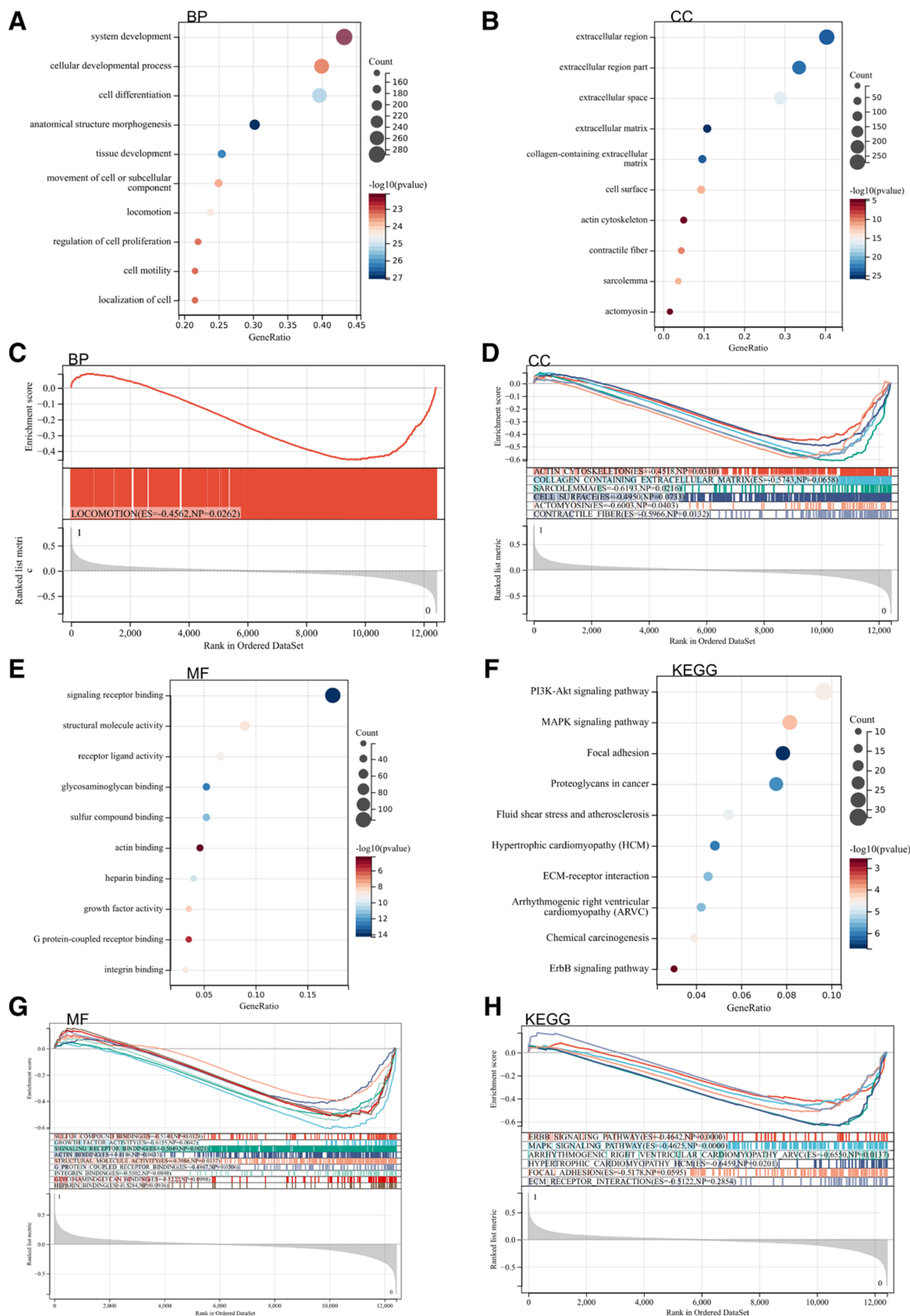

Figure 2. Functional enrichment analysis. (A, B, E, F) Functional enrichment analysis of DEGs. (C, D, G, H) GSEA. DEGs = differentially expressed genes, GSEA = gene set enrichment analysis.

2.11.9. Signal detection. An appropriate substrate, such as horseradish peroxidase substrate for enzymatic detection or fluorescence for fluorescently labeled antibodies, is added to generate a detectable signal.

2.11.10. Imaging and analysis. Using imaging equipment such as a chemiluminescence imager or fluorescent imaging system, protein bands are captured. Comparing band intensity and size provides information about protein expression levels.

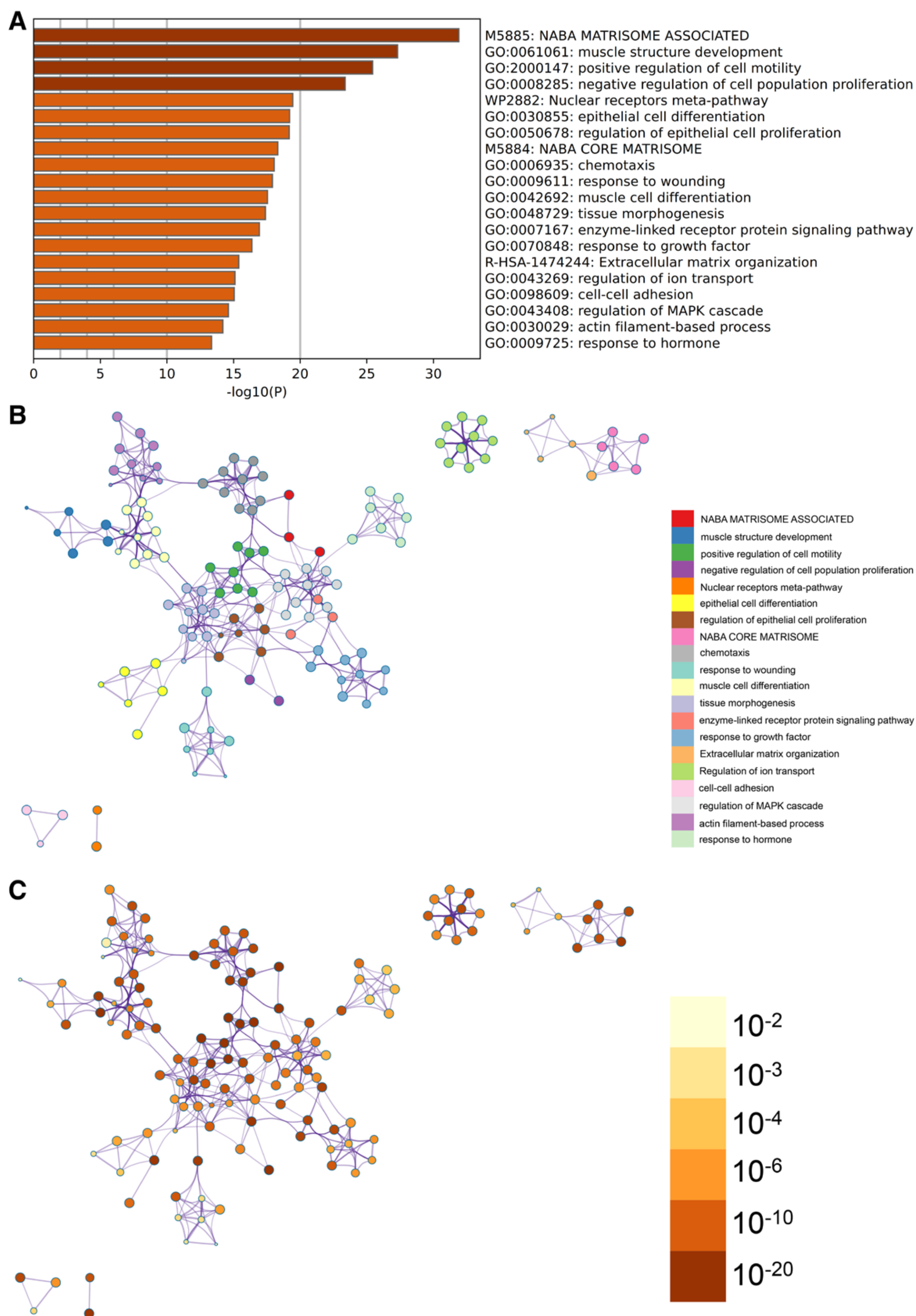

Figure 3. Metascape enrichment analysis. (A) The enzyme-linked receptor protein signal pathway and nuclear receptor meta-pathway can be seen in the GO enrichment project. (B) Enrichment networks colored by enrichment terms. (C) Enrichment networks colored by *P* values. GO = Gene Ontology.

2.12. The miRNA

TargetScan is a bioinformatics tool and database for molecular biology and genomics, specifically designed to predict animal microRNA (miRNA) target genes. TargetScan analyzes the sequence of a given mRNA and predicts potential binding sites for miRNAs. Screening of miRNAs regulating central DEGs was performed using TargetScan.

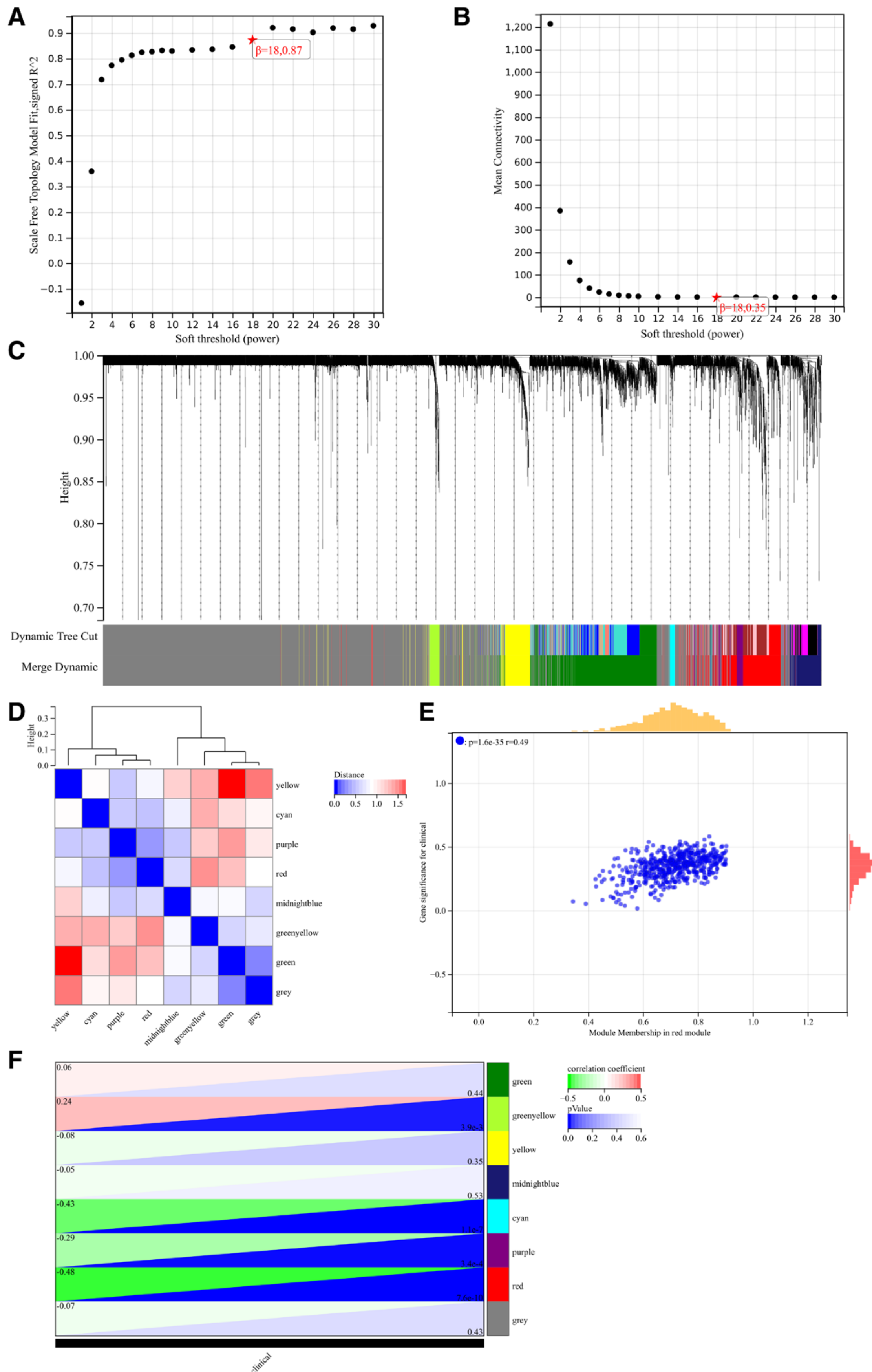

Figure 4. WGCNA. (A) β = 18,0.87. (B) β = 18,0.35. (C) The hierarchical clustering tree of all genes is constructed and 3 important modules are generated. (D) The interaction between these modules. (E) GS-MM correlation scatter map of related hub genes. (F) The module-phenotypic correlation heat map. WGCNA = Weighted Gene Co-Expression Network Analysis.

3. Results

3.1. Differential gene analysis

According to set cutoff value and the de-batch merging matrix of GSE114740 and GSE200879, 770 DEGs were identified (Fig. 1).

3.2. Functional enrichment analysis

3.2.1. DEGs. We analyzed these DEGs by GO and KEGG. According to GO, they were mainly concentrated in cellular developmental process, cell differentiation, tissue development, regulation of cell proliferation, extracellular, cell surface, actin cytoskeleton, actin binding and G protein coupled receptor

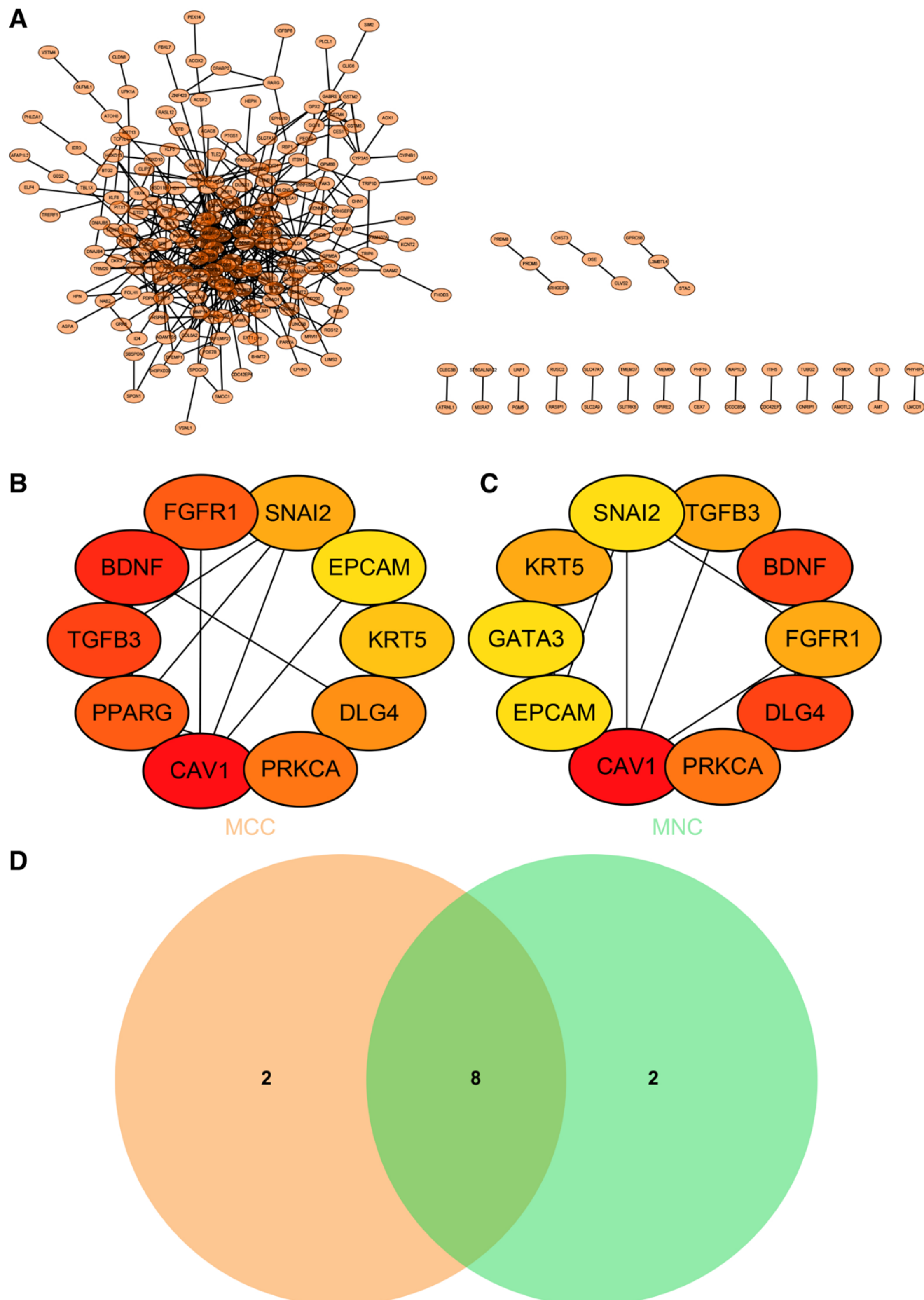

Figure 5. Construction and analysis of protein–protein interaction (PPI) network. (A) PPI network. (B) MCC was used to identify central genes. (C) MCC was used to identify central gene. (D) Wayne graph merging.

binding. In KEGG analysis, they were mainly concentrated in PI3K-Akt signal pathway, MAPK signal pathway and ErbB signal pathway (Fig. 2A, B, E, and F).

3.2.2. GSEA. GSEA was performed to search for possible enrichment items among non-differentially expressed genes, and results of DEGs were verified. The intersection of enrichment items and GOKEGG enrichment items of differentially expressed genes is shown in the figure, which is mainly concentrated in actin cytoskeleton, collagen-containing extracellular matrix, sarcolemma, cell surface, actomyosin, contractile fiber, sulfur compound binding, growth factor activity, signaling receptor binding, actin binding, structural molecule activity, G protein-coupled receptor binding, integrin binding, glycosaminoglycan binding, heparin binding, ErbB signaling pathway, MAPK signaling pathway, Arrhythmogenic right ventricular cardiomyopathy (ARVC), Hypertrophic cardiomyopathy (HCM), Focal adhesion and ECM-receptor interaction (Fig. 2C, D, G, and H).

3.3. Metascape enrichment analysis

In the metascape enrichment project, the enzyme-linked receptor protein signal pathway and nuclear receptor meta-pathway can be seen in the GO enrichment project (Fig. 3A). At the same time, we also output the enrichment network colored by enrichment term and *P*-value (Fig. 3B and C), which visually represents the correlation and confidence of each enrichment project.

3.3.1. WGCNA. The network topology is analyzed and soft threshold power of WGCNA is set to 9, which is lowest power of scale-free topology fitting index of 0.9 (Fig. 4A and B). The hierarchical clustering tree of all genes were constructed, three important modules were generated (Fig. 4C). Then analyze interaction between these modules (Fig. 4D). The module-phenotypic correlation heat map (Fig. 4F) and the GS-MM correlation scatter map of related hub genes were generated (Fig. 4E).

3.4. The PPI network

The PPI network is constructed from STRING online database and analyzed by Cytoscape software (Fig. 5A). Identification of hub genes by 2 different algorithms (Fig. 5B and C) and Wayne graph merging (Fig. 5D), 8 core genes (CAV1, BDNF, TGFB3, FGFR1, PRKCA, DLG4, SNAI2, KRT5) are obtained.

At the same time, we also use the metascape website to output the protein interaction network, and identify the core module to verify the PPI network results in STRING. Among them, CAV1, TGFB3, FGFR1, SNAI2, KRT5 were identified as core genes.

3.5. Gene expression heat map

The expression heat map of core genes in samples was visualized (Fig. 6). There was no significant difference in expression of core genes (BDNF, PRKCA, DLG4) between prostate cancer tissues and normal tissues. Core genes (CAV1, TGFB3, FGFR1, SNAI2, KRT5) are highly expressed in prostate cancer tissues and low in normal tissues.

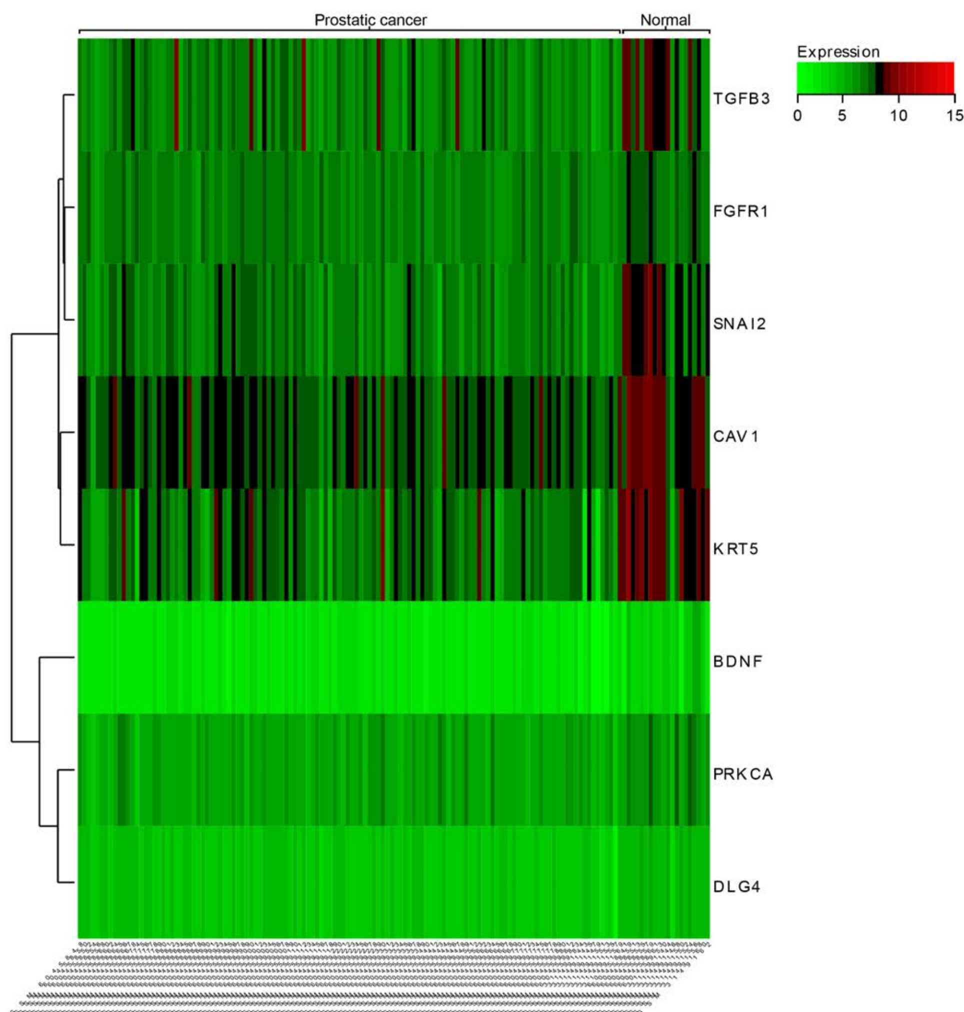

Figure 6. Gene expression heat map.

3.6. Immune infiltration analysis

We used CIBERSORT software package to analyze the de-batch merging matrix of GSE114740 and GSE200879. Under 95% confidence, we obtained proportion of immune cells in the whole gene expression matrix (Fig. 7A) and heat map of immune cell expression in data set (Fig. 7B). We also analyzed the correlation of infiltrating immune cells and obtained the co-expression pattern among immune cell components (Fig. 7C).

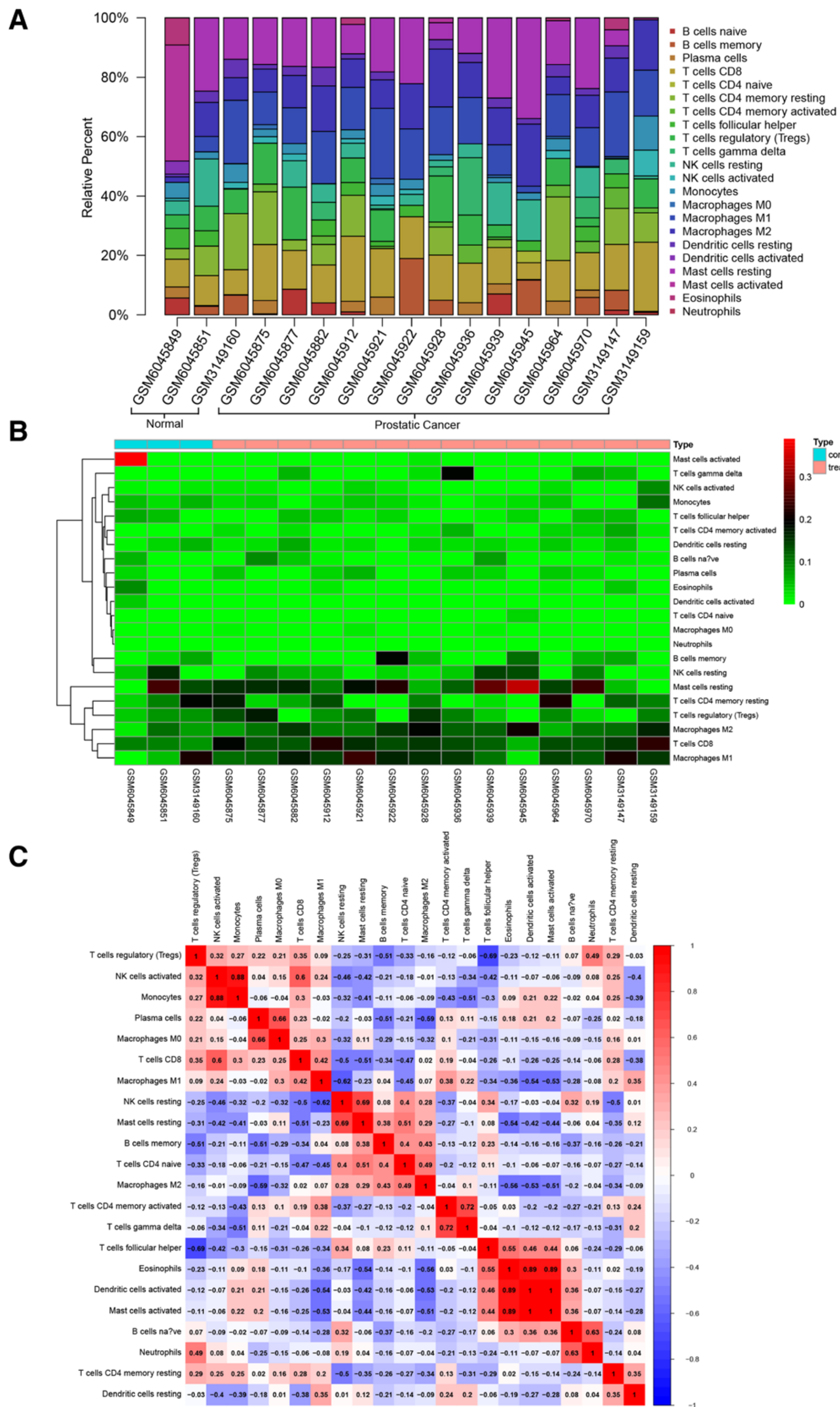

Figure 7. Immune infiltration analysis. (A) The proportion of immune cells in the whole gene expression matrix. (B) The heat map of immune cell expression in the data set. (C) The co-expression pattern among immune cell components.

3.7. The CTD analysis

Core genes was entered into CTD to find diseases related to core genes. Core genes (CAV1, TGFB3, FGFR1, SNAI2, KRT5) were found to be associated with prostate tumor, cancer, tumor metastasis, necrosis and inflammation (Fig. 8).

3.8. Western blot verified

The expression levels of CAV1, KRT5, IGF-I, IGF-IR, PI3K, PDK-1 and EGFR were higher in prostate cancer than in normal control group, higher in prostate cancer-over expression (OE) than in prostate cancer group, and lower in prostate cancer-knock out (KO) than in prostate cancer group (Fig. 9). The expression levels of P53 and IL-10 were lower in prostate cancer than in normal control group, higher in prostate cancer-OE than in prostate cancer group, and lower in prostate cancer-KO than in cancer group (Fig. 10). The expression levels of MMP-2 and Cyclin-D1 were higher in prostate cancer than in normal control group, higher in prostate cancer-OE than in prostate cancer group, and lower in prostate cancer-KO than in prostate cancer group. (Fig. 11). The knock out assay and over expression assay were successful (*$P < .05$).

3.9. The miRNA prediction and functional annotation related to hub gene

Hub genes were input into TargetScan to search for related miRNAs (Table 1). We found that the related miRNA of CA V1 gene is hsamiR-124-3p.1, the related miRNA of mirnahsa-miR-133a-3p.1. KRT5 gene is hsa-miR-325-3p, the related miRNA of hsa-miR-340-5pscape SNAI2 gene is hsa-miR203a-3p.2. TGFB3 gene, and the related miRNA of hsa-miR203a-3p.2. TGFB3 gene is hsa-miR-203a-3p.1.

4. Discussion

Globally, prostate cancer is the most common cancer among men, particularly prevalent in developed countries.[17,18] High morbidity and mortality have caused a huge economic and medical burden on individual families and society. The main result of this study was that CAV1 and KRT5 were highly expressed in prostate cancer. The higher expression of CAV1 and KRT5, worse the prognosis.

Caveolin-1, a scaffold protein encoded by CAV1, is a major membrane intrinsic protein in hole-like invagination (caveolae) on the cell surface, which plays a certain role in maintaining the integrity of caveolae, cell transport and signal transduction.[19]

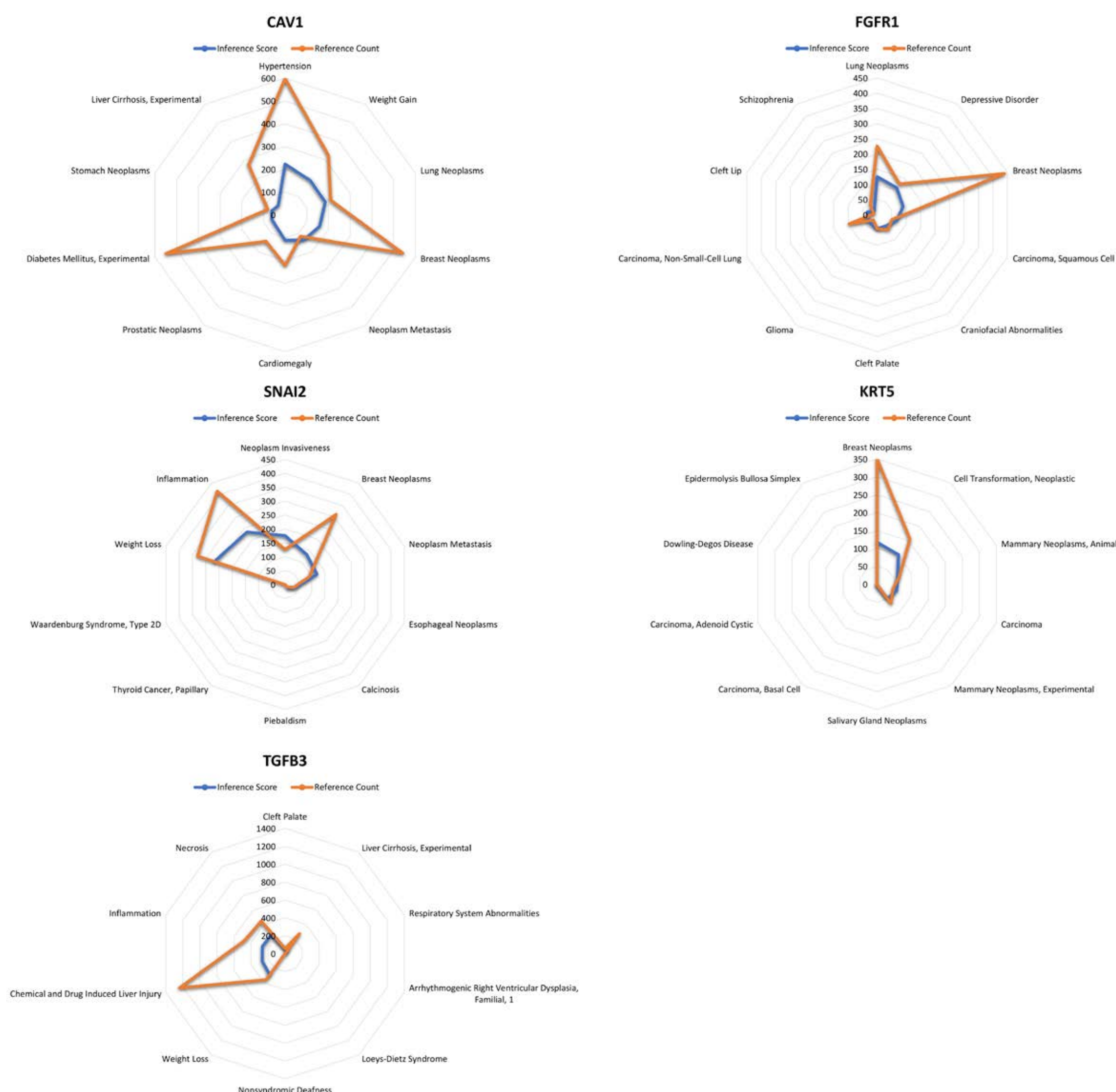

Figure 8. CTD analysis. Core genes (CAV1, TGFB3, FGFR1, SNAI2, KRT5) were found to be associated with prostate tumor, cancer, tumor metastasis, necrosis and inflammation. CTD = comparative toxicogenomics database.

Microcapsule is a special intracellular depression on the surface of lipid raft on cell membrane. Microcapsule protein 1 (caveolin-1) is an integrated membrane protein on the cell membrane. It is the main component of microcapsule formation and is highly expressed in many cells. Microcapsules and caveolin-1 play an important role in regulating substance transport, endothelial infiltration and tumorigenesis.[20] Importantly, CAV-1 is the medium of many signaling pathways. NF- κ B is a polyprotein complex, and NF- κ Bp65 (RELA) is one of its most important components.[21,22] As a major transcription factor, NF- κ Bp65 is involved in regulation of various inflammatory mediators, inflammation plays an important role in tumor development.[23] CAV-1 may be a tumor suppressor gene, and its mutation has been detected in human tumors. Mahdieh Aliyari et al showed that Caveolin-1 is highly expressed in prostate cancer (PC) and is associated with disease progression.[24] Jaromir Gumulec et al found no significant difference in Cav-1 between prostate patients and control group. However, the Cav-1 of high

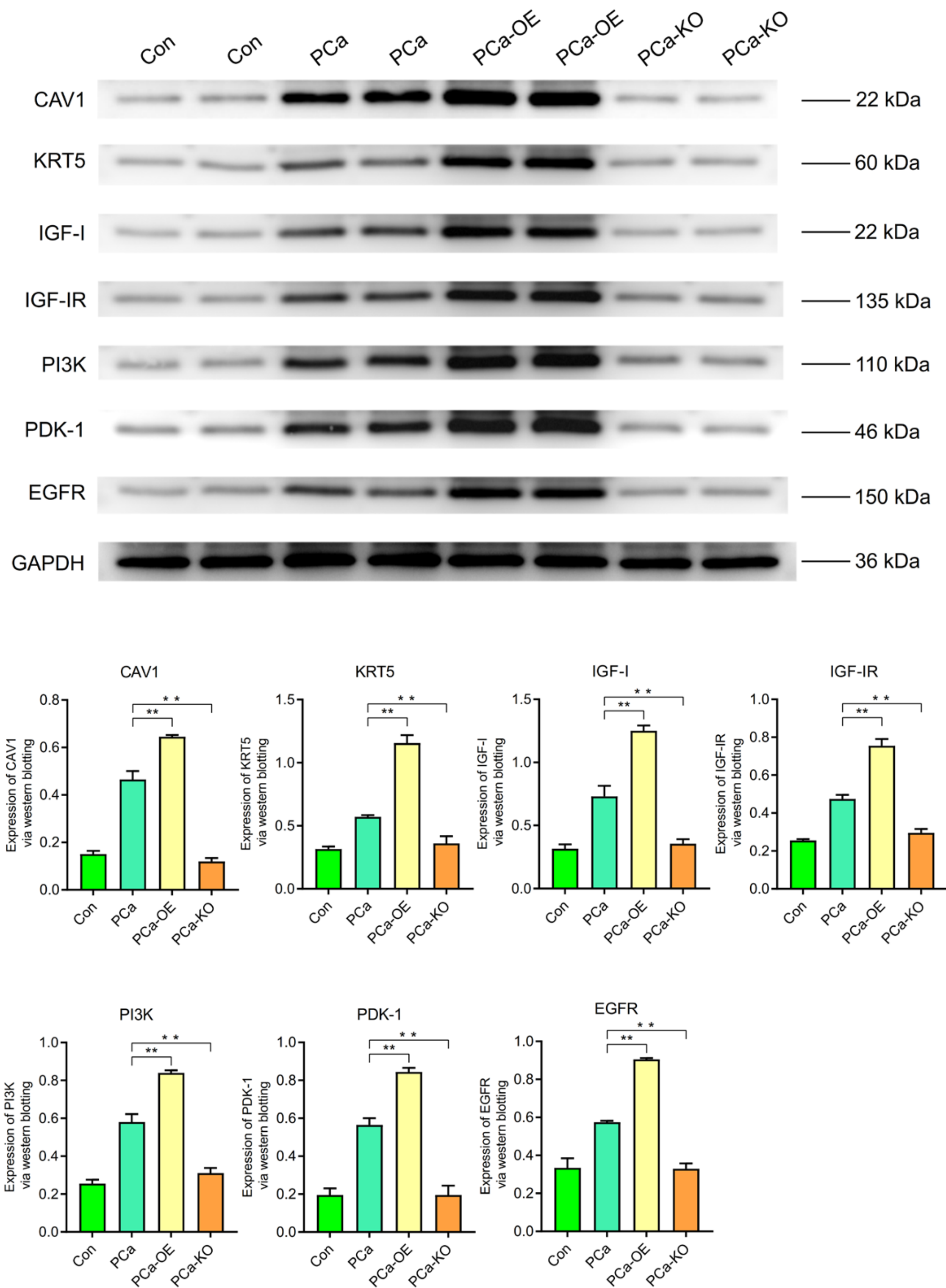

Figure 9. CAV1, KRT5, IGF-I, IGF-IR, PI3K, PDK-1, and EGFR were higher in prostate cancer via WB assay. *$P < .05$. WB = western blot.

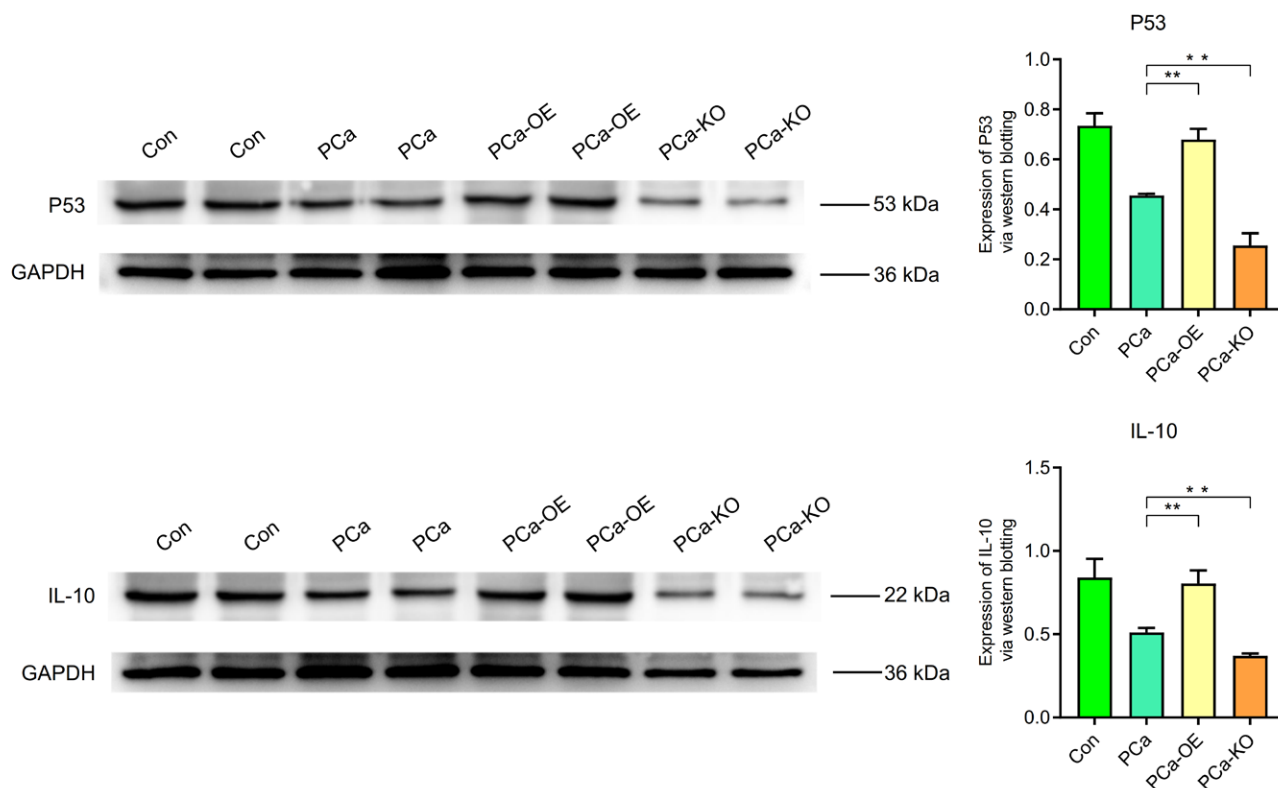

Figure 10. P53 and IL-10 were lower in prostate cancer. *P < .05.

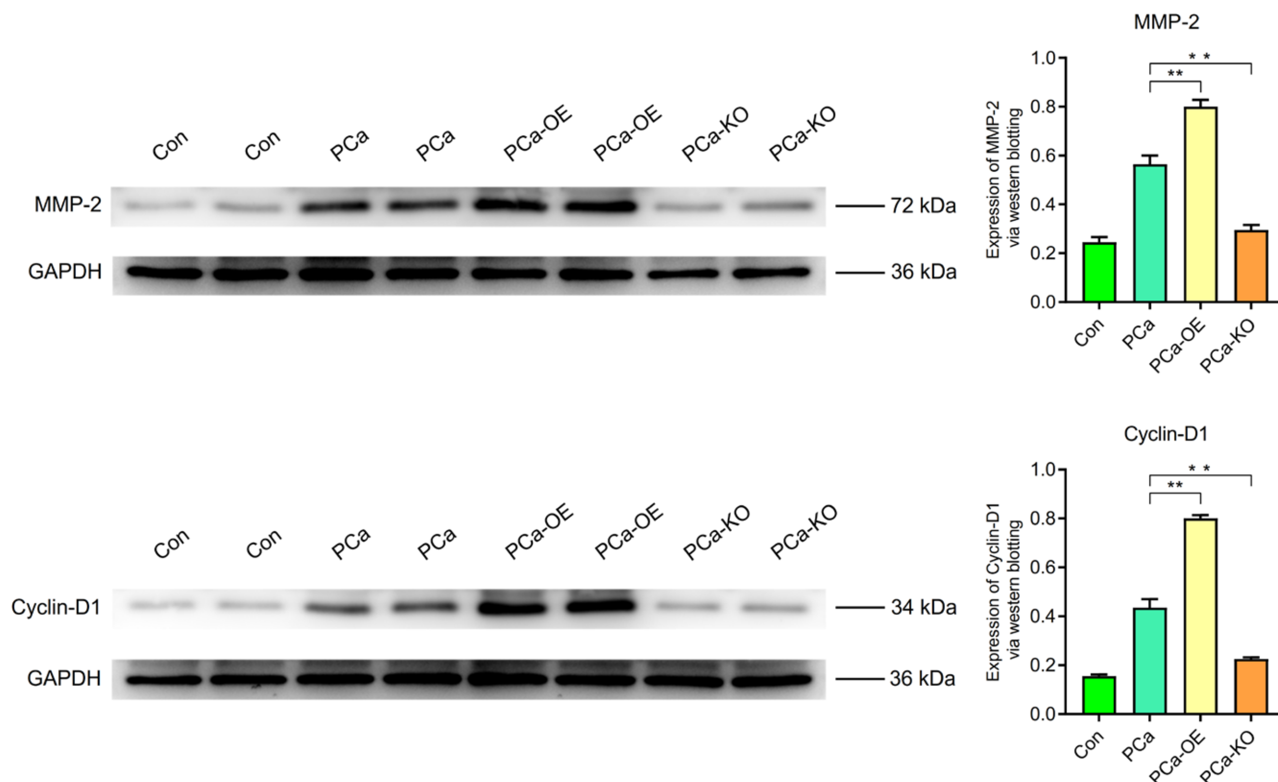

Figure 11. MMP-2 and Cyclin-D1 were higher in prostate cancer. *P < .05.

tumor stage (TNMT4) was 2.8 times higher than that of lower stage, positively correlated with histological grade. In addition, it was also found that the body's antioxidant capacity decreased in patients with high serum Cav-1 levels.[25] Cancer stem cell (CSC) subsets play a key role in cancer progression, recurrence and treatment of drug resistance. Although only a few genetically preprogrammed cells in each organ have stem cell capacity, CSCs appears to be inducible in heterogeneous tumor cell

Table 1

A summary of miRNAs that regulate hub genes.

	Gene	miRNA	
1	CAV1	hsa-miR-124-3p.1	
2	FGFR1	hsa-miR-133a-3p.1	
3	KRT5	hsa-miR-325-3p	hsa-miR-340-5p
4	SNAI2	hsa-miR-203a-3p.2	
5	TGFB3	hsa-miR-203a-3p.1	

populations. In addition, mechanism of Cav-1 promoting EMT and NED phenotype through NF κ B signal pathway was also described.[26] In prostate cancer, aberrant CAV1 expression is associated with alterations in cellular signaling pathways that may drive cancer cell growth and differentiation. Relevant literature has reported that the main functions of Cav1 in the prostate cancer microenvironment are to promote angiogenesis and cell survival. Abnormal Cav1 expression leads to faster progression of prostate cancer and is not conducive to treatment.[27] The above literature review is consistent with our results, and based on above literature analysis, we speculate that CAV1 may play an important role in occurrence and development of prostate cancer, but its mechanism of action on prostate cancer needs to be further explored.

The KRT gene encodes an intermediate filament protein that constitutes the cytoskeleton of epithelial cells from which malignant cells typically originate.[28] KRT may play a role in apoptosis, cell growth, epithelial polarity, wound healing and tissue remodeling. Recent studies have shown that KRT gene is the most common and specifically expressed gene in epithelial cells, and its abnormal expression in different cancers affects cell proliferation, invasion and migration.[29,30] In terms of urothelial cells, breast cancer and lung cancer, KRT is often used to determine the origin of cancer cells and provide some guidance for diagnosis. KRT is also involved in the regulation of cell signal transduction, protein synthesis and the maintenance of polarized cell structure. KRT5 has been used as a single marker or in combination with KRT6 (KRT5/6) as part of the antigen-specific immunohistochemical diagnosis of squamous cell carcinoma. In bladder cancer, KRT5/6 and KRT20 are used as a combined marker for immunohistochemical analysis, which can help clinically evaluate the benefits of chemotherapy. The defect of KRT5 gene in SK-OV-3 cells can prevent cell migration. The expression of KRT5 and Trp53 mutation in muscle cells of mice with squamous differentiation lead to a higher incidence of invasive bladder cancer.[31] Tianyi Wei et al show that KRT5 has potential clinical diagnosis and prognostic value, and can be used as a new candidate biomarker and therapeutic target for prostate cancer. In addition, accumulated evidence suggests that KRT5 is involved in development of many types of cancer. Breyer et al proved that the expression of KRT5 has a strong correlation with the recurrence and metastasis of non-muscular invasive bladder cancer.[32] Another study shows that KRT5 can regulate cytoskeleton formation and venous infiltration of cancer.[33] Du hong bing et al found that the down-regulation of miR-601 reduces rate of proliferation, invasion and metastasis of prostate cancer stem cells by involving the interaction between miR-601 and KRT5, and highlighting potential value of miR-601 and KRT5 in treatment of prostate cancer.[34] In prostate cancer, KRT5 may be related to maintaining the structural integrity and stability of cells, and the abnormal expression of KRT5 may be related to the heterogeneity of prostate cancer, that is, different parts of the tumor cells may express different cytoskeletal proteins, which may affect the biological behavior of the tumor. Based on above findings, we speculate that KRT5 may play an important role in the progression of prostate cancer. However, the mechanism of its action on prostate cancer needs to be further explored.

Although this paper has carried out bioinformatics analysis, there are still some shortcomings. Animal experiments with overexpression or knockdown of the gene were not performed in this study to further verify its function. Therefore, this aspect should be explored in depth in future studies.

5. Conclusion

The expression of CAV1 and KRT5 is low in patients with prostate cancer, and may play a significant role in the development of prostate cancer through inflammation and signal transduction. CAV1 and KRT5 may be molecular targets of prostate cancer, and provide a basis for the study of the mechanism of prostate cancer.

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