**Open Access Library Journal**
2023, Volume 10, e9747
ISSN Online: 2333-9721
ISSN Print: 2333-9705

# Identification of Hub Genes in Prostate Cancer by Bioinformatics Analysis

**Rui Zhang[1,2], Wenhua Guo[3], Luhong Yang[1,2*]**

[1]Modern College of Humanities and Science of Shanxi Normal University, Linfen, China
[2]School of Life Science, Shanxi Normal University, Linfen, China
[3]People's Government of Zuoyi Town, Guangling County, Datong, China
Email: *ylh1010309@126.com

**How to cite this paper:** Zhang, R., Guo, W.H. and Yang, L.H. (2023) Identification of Hub Genes in Prostate Cancer by Bioinformatics Analysis. *Open Access Library Journal*, **10**: e9747.
https://doi.org/10.4236/oalib.1109747

**Received:** January 11, 2023
**Accepted:** March 28, 2023
**Published:** March 31, 2023



## Abstract

**Objective:** To identify the candidate hub genes of prostate cancer (PCa) and investigate the relevance of the genes on the development of PCa by bioinformatics methods. **Methods:** The mRNA expression profile datasets GSE103512 was collected from GEO database, and find out differential expression genes (DEGs) between PCa and normal tissues using the GEO2R tool. Subsequently, to further elucidate the interaction of DEGs and screen the hub genes, we conducted GO and KEGG enrichment analysis by DAVID 6.8 database, and constructed protein-protein interaction (PPI) network by the STRING database. The GEPIA database was utilized to analyze the expression levels of hub genes in PCa and normal tissues. **Results:** A total of 755 DEGs were identified, including 211 upregulated genes and 544 downregulated genes. GO analysis was mainly enriched in extracellular exosome, glutathione metabolic process, and composition of organelle membranes. Fatty acid metabolism, metabolic pathways, and cGMP-PKG signaling pathways were mainly enriched signaling pathways based on KEGG analysis. Ten hub genes were obtained by analyzing the PPI network using cytoHubba plug-in of Cytoscape software. CDH1, CD24, ACACA, and SCD were upregulated in PCa tissues, whereas VEGFA was downregulated in PCa tissues. **Conclusion:** 10 hub genes of PCa were screened out by bioinformatical analysis in this study and are expected to play crucial roles in the treatment of PCa.

## Subject Areas

Bioinformatics

## Keywords

Prostate Cancer (PCa), DEGs, Bioinformatics Analysis

## 1. Introduction

Prostate cancer (PCa) is the most frequent tumor in men worldwide and the second leading cause of mortality among males in Western countries [1] [2]. In China, the morbidity and mortality of PCa have rapidly increased in recent years, which is recognized as a leading and increasing health problem [3] [4]. Although the etiology of PCa is unclear yet, age, family history, race, lifestyle, and environmental factors are defined as risk factors for the development of disease [5]. The development of PCa mostly depends on the increased cell proliferation, and metastasis is often responsible for the recurrence, unsatisfactory prognosis, and high mortality of PCa [4] [6]. PCa is typically treated by radical prostatectomy (surgery), hormonal therapy, chemotherapy, and radiation therapy. However, these methods can have adverse effects on patients [7].

With the rapid development of biotechnology and sequencing technology, bioinformatics analysis has been extensively used to screen and identify key biomarkers and potential molecular mechanisms of some diseases [8]. Gene Expression Omnibus (GEO) is a public database provided by the National Center for Biotechnology Information (NCBI) in 2000 that contains a massive amount of gene chip expression data in various diseases, and the GEO datasets could be used to determine differentially expressed genes (DEGs) [9].

In this study, to obtain the potential biomarkers for the diagnosis and treatment of PCa, the gene expression profile dataset GSE103512 was collected from the GEO database. Then, DEGs were screened between PCa samples and normal samples using the web tool GEO2R. The functional enrichment and network analysis of the DEGs were performed. Finally, we obtained the hub genes, which may offer inspiration for more in-depth research in prostate cancer.

## 2. Materials and Methods

### 2.1. Datasets Selecting and DEGs Identification

The gene expression dataset GSE103512 used in this study was obtained from NCBI Gene Expression Omnibus (GEO) database (https://www.ncbi.nlm.nih.gov/geo/). It contains 280 samples about normal and tumor samples of four cancer types, and we analyzed 60 PCa samples and 7 normal prostate samples.

Using the GEO2R (http://www.ncbi.nlm.nih.gov/geo/geo2r) online data analysis tool to identify the differentially expressed genes (DEGs) between PCa and normal samples. $|\log FC| > 1$ and $P < 0.05$ were considered as statistically significant for the DEGs, we defined upregulation as $\log FC > 1$ and downregulation as $\log FC < -1$ [10]. Volcano plot of the DEGs was generated using the ggplot2 package in R software (version3.6.3).

### 2.2. GO and KEGG Analysis of DEGs

GO and KEGG enrichment analysis were conducted using the DAVID 6.8 database (https://david.ncifcrf.gov/), setting the species to "Homo sapiens" and $P <$

0.05 was considered to indicate a statistically significant difference [11]. The results were visualized by ggplot2 package in R (version3.6.3).

### 2.3. PPI Network Construction and Hub Genes Identification

The STRING database 11.5 (https://www.string-db.org/) was utilized to construct the PPI network of DEGs. The organism selected for analysis was "Homo sapiens" and the interaction score was set to a medium confidence of 0.4 [10]. Subsequently, cytoHubba plugin in Cytoscape software (version 3.7.2) was used to visualize the hub genes in the PPI network by importing the TSV file of the STRING database.

### 2.4. Expression Analysis of Hub Genes in PCa

GEPIA database (http://gepia.cancer-pku.cn/) is a comprehensive online tool that integrates TCGA cancer big data and GTEx normal tissue projects [12]. In our study, GEPIA was employed for analyzing the expression levels of hub genes in PCa and normal tissues.

## 3. Results

### 3.1. Screening of DEGs

During an analysis of the GSE103512 dataset, a total of 755 DEGs were identified by using the GEO2R online tool, including 211 upregulated genes and 544 downregulated genes (**Figure 1**).

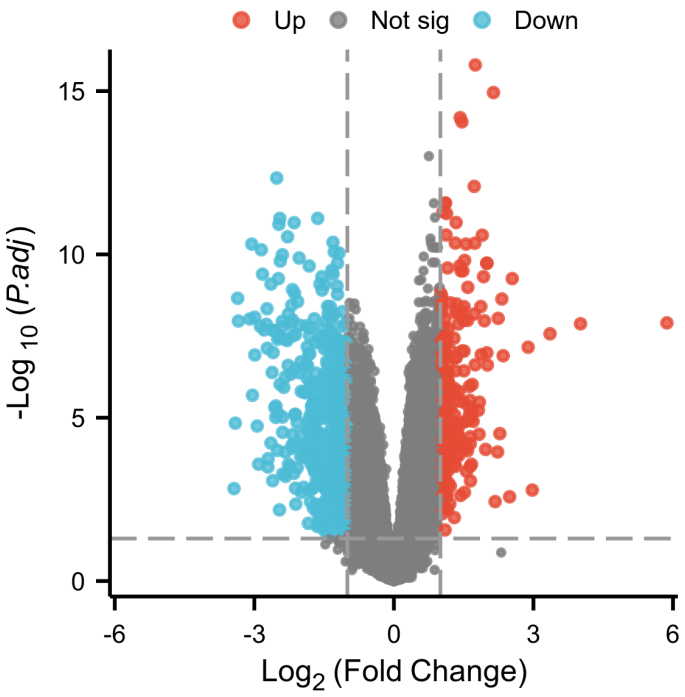


**Figure 1.** Volcano plot of the DEGs. Blue dots indicate downregulated genes, red dots indicate upregulated genes and grey dots indicate not significant genes. X-axis represents fold change ($log_2$) and Y-axis represents P ($-log_{10}$).

### 3.2. Functional Annotation of DEGs

The 755 DEGs were imported into DAVID for GO and KEGG pathway analysis with a setting of $P < 0.05$. We obtained 158 GO terms and the top 15 terms from biological process (BP), cellular component (CC) and molecular function (MF) ranked by P-value were visualized (Table 1, Figure 2).

**Table 1.** GO enrichment analysis.

| Ontology | Description | Gene counts | P-value |
|---|---|---|---|
| BP | GO:0043066~negative regulation of apoptotic process | 34 | 4.21E−07 |
| BP | GO:0001666~response to hypoxia | 18 | 1.63E−06 |
| BP | GO:0010628~positive regulation of gene expression | 31 | 7.83E−06 |
| BP | GO:0098609~cell-cell adhesion | 16 | 4.88E−05 |
| BP | GO:0010629~negative regulation of gene expression | 21 | 6.50E−05 |
| CC | GO:0070062~extracellular exosome | 144 | 2.67E−32 |
| CC | GO:0005576~extracellular region | 89 | 2.30E−08 |
| CC | GO:0005615~extracellular space | 81 | 1.20E−07 |
| CC | GO:0016020~membrane | 132 | 2.15E−07 |
| CC | GO:0048471~perinuclear region of cytoplasm | 41 | 1.06E−06 |
| MF | GO:0042802~identical protein binding | 74 | 7.51E−07 |
| MF | GO:0005178~integrin binding | 15 | 3.12E−05 |
| MF | GO:0003779~actin binding | 21 | 1.89E−04 |
| MF | GO:0008236~serine-type peptidase activity | 8 | 4.78E−04 |
| MF | GO:0098641~cadherin binding involved in cell-cell adhesion | 5 | 7.37E−04 |

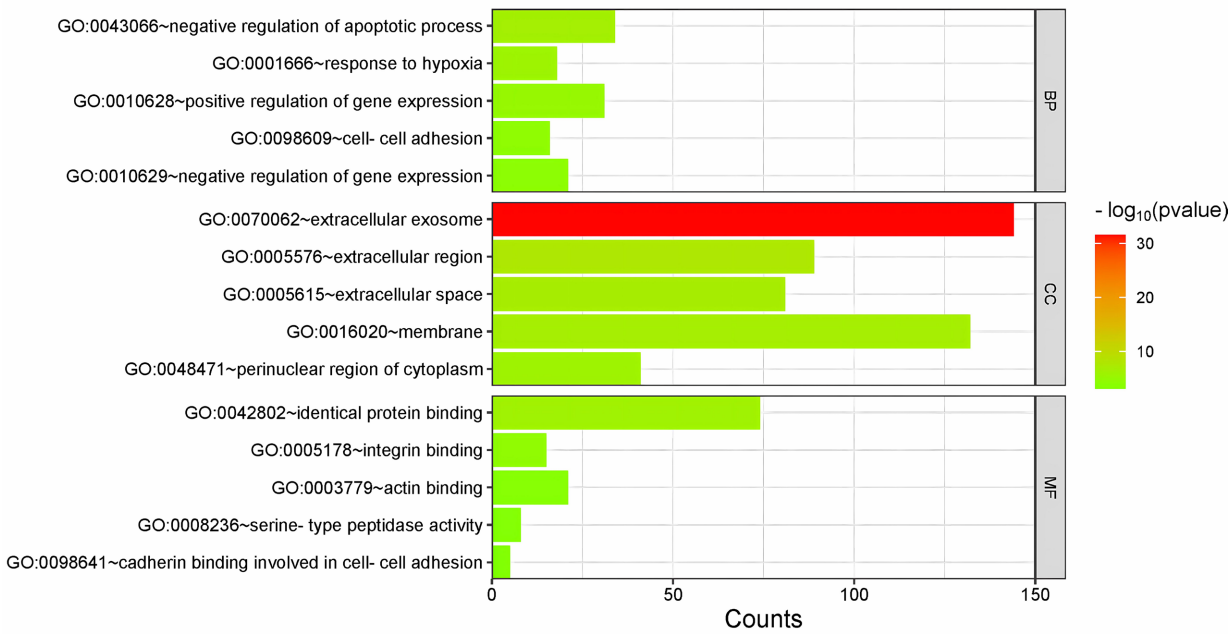


**Figure 2.** Bar charts of GO terms. The x-axis represents the number of genes and the y-axis represents the GO terms. Red, green, and blue boxes represent GO terms of BP, CC, and MF, respectively.

KEGG analysis revealed that DEGs were enriched in 14 pathways, the top 10 enrichment pathways were shown (Table 2, Figure 3). Fatty acid metabolism, glutathione metabolism, and metabolic pathways were mainly enriched signaling pathways.

### 3.3. PPI Network and Hub Genes Analysis

In order to analyze the interaction between these DEGs in PCa, the PPI network was constructed by the STRING database (Figure 4). We constructed a network contained 431 nodes and 1370 edges with the interaction score set to 0.4 and hide the disconnect nodes. Furthermore, the top 10 hub genes in the PPI network were identified based on the MCC method by the cytoHubba plugin of Cytoscape (Figure 5).

Table 2. KEGG pathways enrichment analysis.

| Pathway | Gene counts | P-value |
|---|---|---|
| hsa01212: Fatty acid metabolism | 10 | 1.87E−05 |
| hsa00480: Glutathione metabolism | 9 | 2.06E−04 |
| hsa00061: Fatty acid biosynthesis | 5 | 6.10E−04 |
| hsa01100: Metabolic pathways | 57 | 0.003046016 |
| hsa04141: Protein processing in endoplasmic reticulum | 14 | 0.003226595 |
| hsa04022: cGMP-PKG signaling pathway | 13 | 0.005089719 |
| hsa04972: Pancreatic secretion | 9 | 0.010282206 |
| hsa04978: Mineral absorption | 6 | 0.013283839 |
| hsa04970: Salivary secretion | 8 | 0.021069272 |
| hsa04974: Protein digestion and absorption | 8 | 0.023588205 |

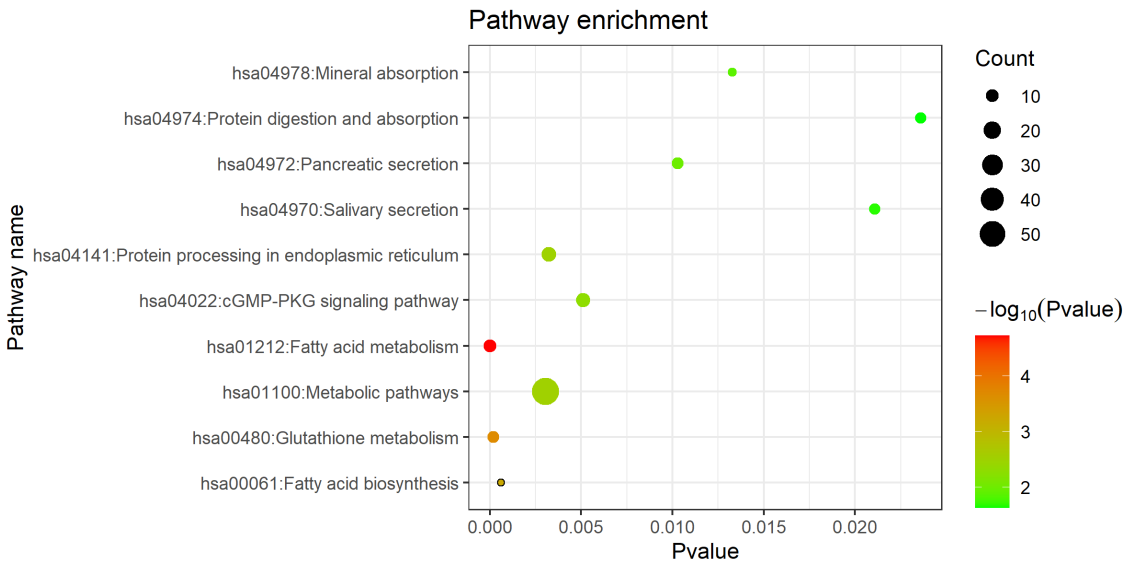


Figure 3. Bubble plot of KEGG pathways enrichment. The x-axis shows P-value and the y-axis shows the names of pathways. The size of the circle represents the number of genes, and the colour represents the P-value.

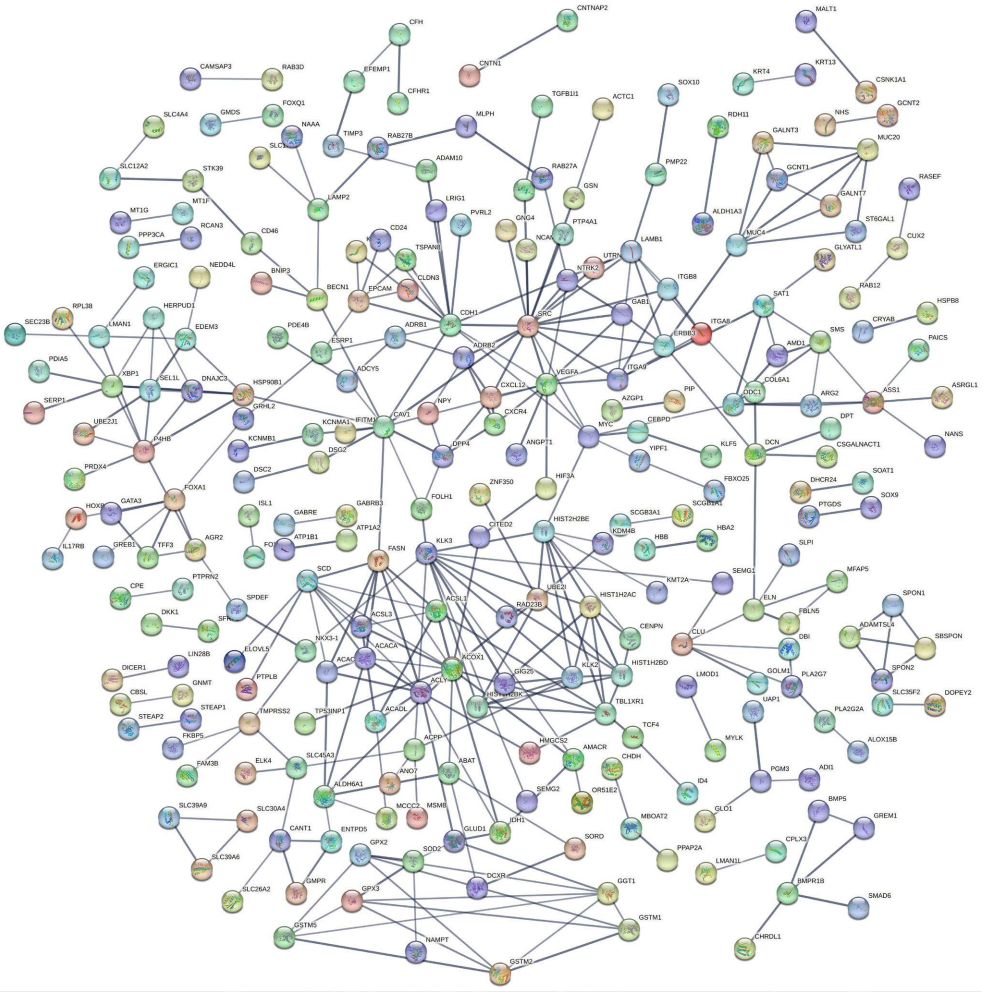

**Figure 4.** PPI network. The nodes represent genes, lines represent the interaction of proteins between genes, and the content within the nodes represent the 3D structure of proteins.

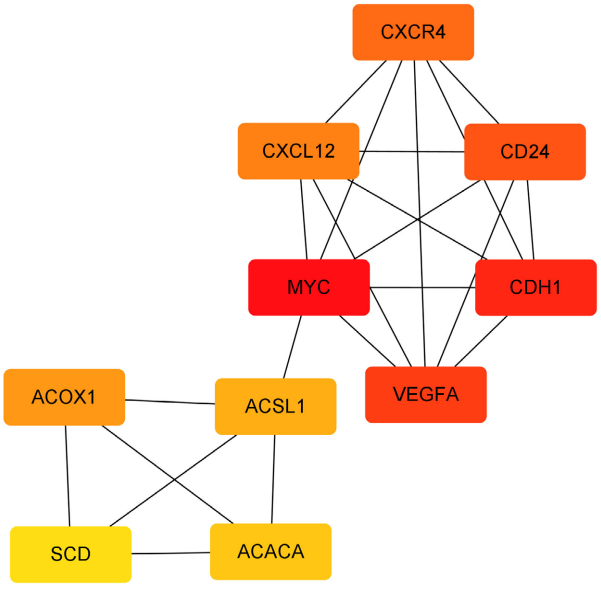


**Figure 5.** Hub genes. The redder the colour of the node, the higher degree of connectivity.

### 3.4. Expression Analysis of Hub Genes

To evaluate the expression level of the hub genes between PCa tissues and normal tissues, the hub genes were analyzed by GEPIA. In the GEPIA datasets, 152 normal tissues and 492 PCa tissues were used for the expression analysis. As presented in **Figure 6**, CDH1, CD24, ACACA, and SCD were obviously upregulated in PCa tissues, whereas VEGFA was downregulated in PCa tissues.

## 4. Discussion

In the present study, we identified 755 DEGs based on the GSE103512 dataset from the GEO database, including 211 up-regulated genes and 544 down-regulated genes. These genes were involved in extracellular exosome, perinuclear region of cytoplasm, negative regulation of apoptotic process, perinuclear region of cytoplasm, serine-type peptidase activity and cadherin binding involved in cell-cell adhesion based on GO analysis.

KEGG analysis revealed that DEGs were mainly involved in pathways like fatty acid metabolism, glutathione metabolism, metabolic pathways, cGMP-PKG signaling pathway. Changes of fatty acid glutathione metabolic pathways have been recognized as hallmarks of cancer, fatty acid metabolism plays an important role in cancer progression, survival, and metastasis [13] [14]. Metabolic pathways are dysregulated in different types of cancer to meet the energetic and biosynthetic demands of cancer cells [15]. cGMP-PKG signaling pathway plays

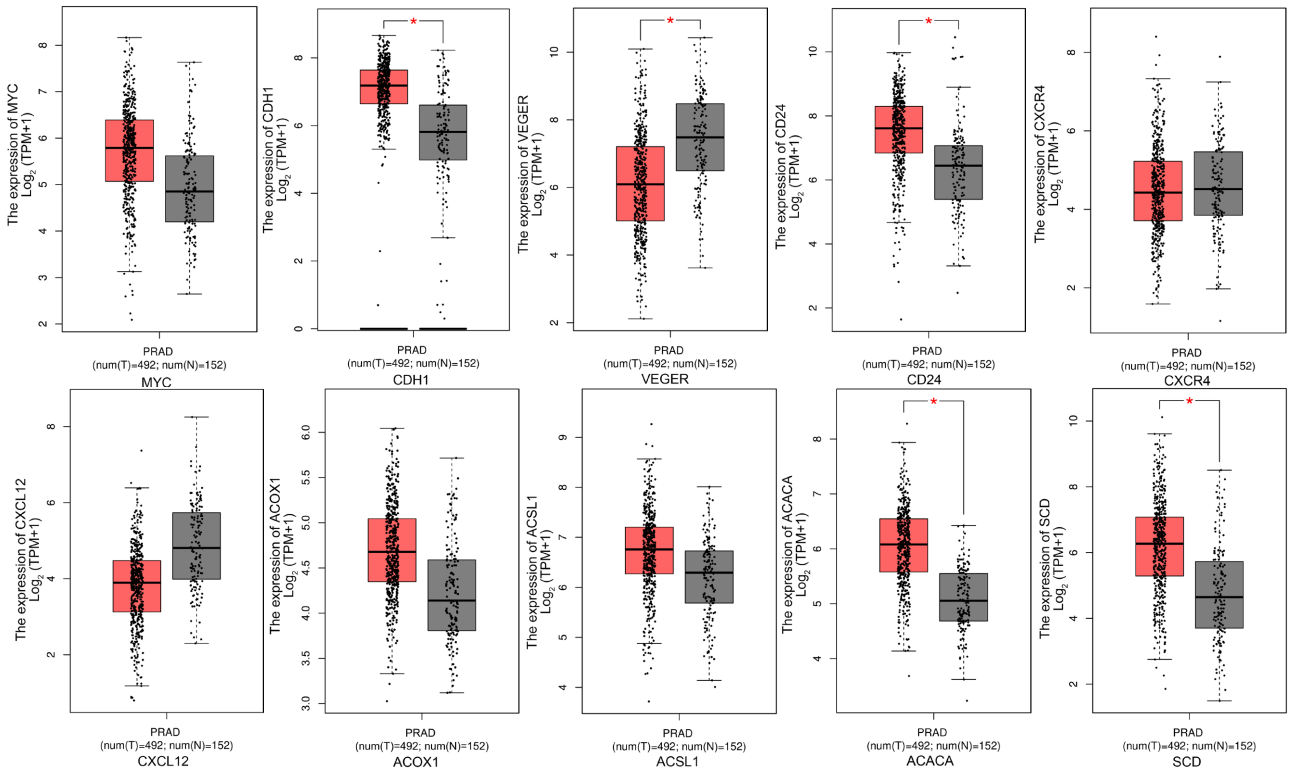


**Figure 6.** Expression analysis of 10 hub genes between PCa and normal tissues based on GEPIA. The red and gray boxes represent tumor and normal tissues, respectively.

an essential role in cell proliferation, survival, cycle progression and apoptosis [16].

Based on the PPI network, we identified 10 hub genes, including *MYC*, *CDH1*, *VEGFA*, *CD24*, *CXCR4*, *CXCL12*, *ACOX1*, *ACSL1*, *ACACA* and *SCD*. *MYC* gene belongs to a group of classical oncogenes, including c-MYC, n-MYC and l-MYC [17], and encodes a nuclear phosphoprotein that plays a role in cell cycle progression, apoptosis and cellular transformation. Amplification of this gene is frequently observed in numerous human cancers. There is evidence to show that MYC was activated at the earliest phases of prostate cancer in prostatic intraepithelial neoplasia, a key precursor lesion to invasive prostatic adenocarcinoma, so MYC is a key role in developing the PCa [17] [18] [19]. *CDH1* encodes a classical cadherin of the cadherin superfamily and loss of or reduced expression of *CDH1* is thought to contribute to more invasive tumors, it was regarded as a critical target in PCa [20]. Gene expression products of *VEGFA* not only stimulate tumor growth, survival and metastasis, but also stimulate hemopoietic cells, endothelial cells and neuronal cells [10]. Some genetic variants in the *VEGFA* gene may influence the risk of high-grade late rectal toxicity after radiotherapy for PCa [21]. *CD24* is over-expressed in cancers and serves as a marker for poor prognosis of PCa [21]. CD24 protected cancer cells escaped engulfing by macrophages and its expression is associated with aggressive and metastatic in PCa [22] [23]. *CXCR4* is over-expressed in PCa, it is a cell surface receptor for the chemokine CXCL12, induction of the CXCL12/CXCR4 axis has been implicated in the progression and metastasis of PCa [24] [25]. Prostate cancer preferentially metastasizes to bone; CXCL12 signaling through CXCR4 enhances the adhesion of PCa cells to bone marrow endothelial cells and stimulates PCa migration toward a CXCL12 gradient [24]. ACOX1 involved in the catabolism of very long–chain fatty acids, saturated long-chain fatty acids involved in the activation of inflammatory and innate immune responses in immune cells [26]. Immune cells and inflammation have vital roles in tumorigenesis to metastasis [27]. ACSL1 involved in the biosynthesis of complex lipids and fatty acid metabolism can enhance tumor progression [28]. Knockdown of *ACACA* expression inhibits cell proliferation in PCa cell-lines [29]. SCD is essential for the survival of cancer cell, also plays a key role in the initiation and progression of PCa [30] [31].

## 5. Conclusion

This study mainly included the acquisition of differentially expressed genes from GSE103512, functional annotation of DEGs, identification of hub genes, and further analysis of the expression level of hub genes between PCa tissues and normal tissues. Here are some conclusions drawn from the study. A total of 755 DEGs were obtained from GSE103512, mainly enriched in some metabolic pathways (fatty acid metabolism, glutathione metabolism and fatty acid biosynthesis). 10 hub genes (*MYC*, *CDH1*, *VEGFA*, *CD24*, *CXCR4*, *CXCL12*, *ACOX1*, *ACSL1*, *ACACA* and *SCD*) were further analyzed, which were expected to have a

certain effect on prostate cancer. Although this study lacked experimental verification, it still provides theoretical guidance in the treatment of PCa.

## Acknowledgements

This work was supported by the grant from Modern College of Humanities and Sciences of Shanxi Normal University (NO. 2020JCYJ19).

## Conflicts of Interest

The authors declare no conflicts of interest.

## References

[1] Jia, Z., Li, W., Bian, P., Liu, H., Pan, D. and Dou, Z. (2020) LncRNA MCM3AP-AS1 Promotes Cell Proliferation and Invasion through Regulating miR-543-3p/SLC39A10/PTEN Axis in Prostate Cancer. *OncoTargets and Therapy*, **13**, 9365-9376. https://doi.org/10.2147/OTT.S245537

[2] Fang, F., Chen, S., Ma, J., Cui, J., Li, Q., Meng, G. and Wang, L. (2018) Juglone Suppresses Epithelial-Mesenchymal Transition in Prostate Cancer Cells via the Protein Kinase B/Glycogen Synthase Kinase-3β/Snail Signaling Pathway. *Oncology Letters*, **16**, 2579-2584. https://doi.org/10.3892/ol.2018.8885

[3] Kong, Z., Wan, X., Lu, Y., Zhang, Y., Huang, Y., Xu, Y., Liu, Y., Zhao, P., Xiang, X., Li, L. and Li, Y. (2020) Circular RNA *circFOXO3* Promotes Prostate Cancer Progression through Sponging miR-29a-3p. *Journal of Cellular and Molecular Medicine*, **24**, 799-813. https://doi.org/10.1111/jcmm.14791

[4] Wang, D., Lu, G., Shao, Y. and Xu, D. (2017) MicroRNA-802 Inhibits Epithelial-Mesenchymal Transition through Targeting Flotillin-2 in Human Prostate Cancer. *Bioscience Reports*, **37**, Article ID: BSR20160521. https://doi.org/10.1042/BSR20160521

[5] Singh, K., Jamshidi, N., Zomer, R., Piva, T.J. and Mantri, N. (2020) Cannabinoids and Prostate Cancer: A Systematic Review of Animal Studies. *International Journal of Molecular Sciences*, **21**, Article No. 6265. https://doi.org/10.3390/ijms21176265

[6] Lu, W., Sun, J., Zhou, H., Wang, F., Zhao, C., Li, K., Fan, C., Ding, G. and Wang, J. (2020) HNF1B Inhibits Cell Proliferation via Repression of SMAD6 Expression in Prostate Cancer. *Journal of Cellular and Molecular Medicine*, **24**, 14539-14548. https://doi.org/10.1111/jcmm.16081

[7] Thambiraj, S., Vijayalakshmi, R. and Ravi Shankaran, D. (2021) An Effective Strategy for Development of Docetaxel Encapsulated Gold Nanoformulations for Treatment of Prostate Cancer. *Scientific Reports*, **11**, Article No. 2808. https://doi.org/10.1038/s41598-020-80529-1

[8] Li, Z., Xu, J., Cui, H., Song, J., Chen, J. and Wei, J. (2020) Bioinformatics Analysis of Key Biomarkers and Potential Molecular Mechanisms in Hepatocellular Carcinoma Induced by Hepatitis B Virus. *Medicine*, **99**, e20302. https://doi.org/10.1097/MD.0000000000020302

[9] Ma, Y., Chen, S.-S., Jiang, F., Ma, R.-Y.and Wang, H.-L. (2021) Bioinformatic Analysis and Validation of microRNA-508-3p as a Protective Predictor by Targeting NR4A3/MEK Axis in Pulmonary Arterial Hypertension. *Journal of Cellular and Molecular Medicine*, **25**, 5202-5219. https://doi.org/10.1111/jcmm.16523

[10] Luo, X., Xu, S., Zhong, Y., Tu, T., Xu, Y., Li, X., Wang, B. and Yang, F. (2019) High Gene Expression Levels of VEGFA and CXCL8 in the Peritumoral Brain Zone Are

Associated with the Recurrence of Glioblastoma: A Bioinformatics Analysis. *Oncology Letters*, **18**, 6171-6179. https://doi.org/10.3892/ol.2019.10988

[11] Guo, W., Zheng, X., Hua, L., Zheng, X., Zhang, Y., Sun, B., Tao, Z. and Gao, J. (2021) Screening and Bioinformatical Analysis of Differentially Expressed Genes in Nasopharyngeal Carcinoma. *Journal of Cancer*, **12**, 1867-1883. https://doi.org/10.7150/jca.48979

[12] Xia, L., Chen, X., Yang, J., Zhu, S., Zhang, L., Yin, Q., Hong, Y., Chen, H., Chen, G. and Li, H. (2020) Long Non-Coding RNA-PAICC Promotes the Tumorigenesis of Human Intrahepatic Cholangiocarcinoma by Increasing YAP1 Transcription. *Frontiers in Oncology*, **10**, Article 595533. https://doi.org/10.3389/fonc.2020.595533

[13] Luo, X., Zheng, E., Wei, L., Zeng, H., Qin, H., Zhang, X., Liao, M., Chen, L., Zhao, L., Ruan, X.Z., Yang, P. and Chen, Y. (2021) The Fatty Acid Receptor CD36 Promotes HCC Progression through Activating Src/PI3K/AKT Axis-Dependent Aerobic Glycolysis. *Cell Death & Disease*, **12**, Article No. 328. https://doi.org/10.1038/s41419-021-03596-w

[14] Sheraj, I., Guray, N.T. and Banerjee, S. (2021) A Pan-Cancer Transcriptomic Study Showing Tumor Specific Alterations in Central Metabolism. *Scientific Reports*, **11**, Article No. 13637. https://doi.org/10.1038/s41598-021-93003-3

[15] Grønningsæter, I.S., Reikvam, H., Aasebø, E., Bartaula-Brevik, S., Tvedt, T.H., Bruserud, Ø. and Hatfield, K.J. (2020) Targeting Cellular Metabolism in Acute Myeloid Leukemia and the Role of Patient Heterogeneity. *Cells*, **9**, Article No. 1155. https://doi.org/10.3390/cells9051155

[16] Wei, J., Shi, Q., Xiong, L., Xin, G., Yi, T., Xiao, Y. and Huang, W. (2021) Transcriptome Profiling of Cells Exposed to Particular and Intense Electromagnetic Radiation Emitted by the "SG-III" Prototype Laser Facility. *Scientific Reports*, **11**, Article No. 2017. https://doi.org/10.1038/s41598-021-81642-5

[17] Pang, K., Zhang, Z., Hao, L., Shi, Z., Chen, B., Zang, G., Dong, Y., Li, R., Liu, Y., Wang, J., Zhang, J., Cai, L., Han, X. and Han, C. (2019) The ERH Gene Regulates Migration and Invasion in 5637 and T24 Bladder Cancer Cells. *BMC Cancer*, **19**, Article No. 225. https://doi.org/10.1186/s12885-019-5423-9

[18] Yeh, H.-Y., Cheng, S.-W., Lin, Y.-C., Yeh, C.-Y., Lin, S.-F. and Soo, V.-W. (2009) Identifying Significant Genetic Regulatory Networks in the Prostate Cancer from Microarray Data Based on Transcription Factor Analysis and Conditional Independency. *BMC Medical Genomics*, **2**, Article No. 70. https://doi.org/10.1186/1755-8794-2-70

[19] Koh, C.M., Bieberich, C.J., Dang, C.V., *et al.* (2010) MYC and Prostate Cancer. *Genes & Cancer*, **1**, 617-628. https://doi.org/10.1177/1947601910379132

[20] Xie, Z.-C., Huang, J.-C., Zhang, L.-J., Gan, B.-L., Wen, D.-Y., Chen, G., Li, S.-H. and Yan, H.-B. (2018) Exploration of the Diagnostic Value and Molecular Mechanism of miR-1 in Prostate Cancer: A Study Based on Meta-Analyses and Bioinformatics. *Molecular Medicine Reports*, **18**, 5630-5646. https://doi.org/10.3892/mmr.2018.9598

[21] Drobin, K., Marczyk, M., Halle, M., Danielsson, D., Papiez, A., Sangsuwan, T., Bendes, A., Hong, M.-G., Qundos, U., Harms-Ringdahl, M., Wersäll, P., Polanska, J., Schwenk, J.M. and Haghdoost, S. (2020) Molecular Profiling for Predictors of Radiosensitivity in Patients with Breast or Head-and-Neck Cancer. *Cancers*, **12**, Article No. 753. https://doi.org/10.3390/cancers12030753

[22] Liu, W., Zhang, Y., Wei, S., Bae, S., Yang, W.-H., Smith, G.J., Mohler, J.L., Fontham, E.T.H., Bensen, J.T., Sonpavde, G.P., Chen, G.Y., Liu, R. and Wang, L. (2020) A

CD24-p53 Axis Contributes to African American Prostate Cancer Disparities. *Prostate*, **80**, 609-618. https://doi.org/10.1002/pros.23973

[23] Xu, K., Meng, Z., Mu, X., Sun, B. and Chai, Y. (2020) One Single Site Clinical Study: To Evaluate the Safety and Efficacy of Immunotherapy with Autologous Dendritic Cells, Cytokine-Induced Killer Cells in Primary Hepatocellular Carcinoma Patients. *Frontiers in Oncology*, **10**, Article 581270. https://doi.org/10.3389/fonc.2020.581270

[24] Frigo, D.E., Sherk, A.B., Wittmann, B.M., Norris, J.D., Wang, Q., Joseph, J.D., Toner, A.P., Brown, M. and McDonnell, D.P. (2009) Induction of Krüppel-Like Factor 5 Expression by Androgens Results in Increased CXCR4-Dependent Migration of Prostate Cancer Cells *in Vitro*. *Molecular Endocrinology*, **23**, 1385-1396. https://doi.org/10.1210/me.2009-0010

[25] Liang, G.-Q., Liu, J., Zhou, X.-X., Lin, Z.-X., Chen, T., Chen, G. and Wei, H. (2020) Anti-CXCR4 Single-Chain Variable Fragment Antibodies Have Anti-Tumor Activity. *Frontiers in Oncology*, **10**, Article 571194. https://doi.org/10.3389/fonc.2020.571194

[26] Moreno-Fernandez, M.E., Giles, D.A., Stankiewicz, T.E., Sheridan, R., Karns, R., Cappelletti, M., Lampe, K., Mukherjee, R., Sina, C., Sallese, A., Bridges, J.P., Hogan, S.P., Aronow, B.J., Hoebe, K. and Divanovic, S. (2018) Peroxisomal β-Oxidation Regulates Whole Body Metabolism, Inflammatory Vigor, and Pathogenesis of Nonalcoholic Fatty Liver Disease. *JCI Insight*, **3**, e93626. https://doi.org/10.1172/jci.insight.93626

[27] Madhavan, S., Gusev, Y., Natarajan, T.G., Song, L., Bhuvaneshwar, K., Gauba, R., Pandey, A., Haddad, B.R., Goerlitz, D., Cheema, A.K., Juhl, H., Kallakury, B., Marshall, J.L., Byers, S.W. and Weiner, L.M. (2013) Genome-Wide Multi-Omics Profiling of Colorectal Cancer Identifies Immune Determinants Strongly Associated with Relapse. *Frontiers in Genetics*, **4**, Article 236. https://doi.org/10.3389/fgene.2013.00236

[28] Chen, W.-C., Wang, C.-Y., Hung, Y.-H., Weng, T.-Y., Yen, M.-C. and Lai, M.-D. (2016) Systematic Analysis of Gene Expression Alterations and Clinical Outcomes for Long-Chain Acyl-Coenzyme A Synthetase Family in Cancer. *PLOS ONE*, **11**, e0155660. https://doi.org/10.1371/journal.pone.0155660

[29] Paul, A., Anand, R., Karmakar, S.P., Rawat, S., Bairagi, N. and Chatterjee, S. (2021) Exploring Gene Knockout Strategies to Identify Potential Drug Targets Using Genome-Scale Metabolic Models. *Scientific Reports*, **11**, Article No. 213. https://doi.org/10.1038/s41598-020-80561-1

[30] Kim, S.-J., Choi, H., Park, S.-S., Chang, C. and Kim, E. (2011) Stearoyl CoA Desaturase (SCD) Facilitates Proliferation of Prostate Cancer Cells through Enhancement of Androgen Receptor Transactivation. *Molecules and Cells*, **31**, 371-377. https://doi.org/10.1007/s10059-011-0043-5

[31] Andrejeva, G., Gowan, S., Lin, G., Wong Te Fong, A.-C.L., Shamsaei, E., Parkes, H.G., Mui, J., Raynaud, F.I., Asad, Y., Vizcay-Barrena, G., Nikitorowicz-Buniak, J., Valenti, M., Howell, L., Fleck, R.A., Martin, L.A., Kirkin, V., Leach, M.O. and Chung, Y.L. (2020) *De Novo* Phosphatidylcholine Synthesis Is Required for Autophagosome Membrane Formation and Maintenance during Autophagy. *Autophagy*, **16**, 1044-1060. https://doi.org/10.1080/15548627.2019.1659608