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Molecular Signature and Prognostic Factors in Papillary Renal Cell Carcinoma through Pathway Enrichment Analysis

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Objectives : Papillary renal cell carcinoma (pRCC) is the second most common subtype of renal cell carcinoma (RCC), with limited molecular characterization and prognostic biomarkers. Identifying key molecular signatures is crucial for understanding disease progression and improving patient outcomes. This study aimed to explore differentially expressed genes (DEGs) and prognostic factors in pRCC using bioinformatics approaches.

Methods : Gene expression data were retrieved from Gene Expression Omnibus (GEO), the publicly available dataset, with accession number GSE15641. DEGs were identified using GEO2R, followed by pathway enrichment analysis using ShinyGO. Protein-protein interaction (PPI) networks were constructed with STRING, and survival analysis was performed using GEPIA2.

Results : A total of 565 DEGs were identified, with 402 upregulated and 163 downregulated genes. Pathway enrichment analysis highlighted the PPAR signaling pathway (FDR = 0.0223) as a key molecular signature, involving genes such as FABP1, GK, HMGCS2, APOC3, LPL, PCK1, and ADIPOQ. Survival analysis using GEPIA2 demonstrated that LPL expression was significantly correlated with patient survival ($p = 0.0079$), suggesting its potential as a prognostic biomarker. Other pathways enriched included PI3K-Akt, MAPK, and metabolic pathways, further supporting their roles in pRCC progression.

Conclusions : In conclusion, this study identifies the PPAR signaling pathway as a critical molecular signature in pRCC and suggests LPL as a potential prognostic biomarker. These findings provide valuable insights into the molecular mechanisms of pRCC and may guide future therapeutic strategies. Further validation in clinical settings is required to confirm their prognostic and therapeutic potential.

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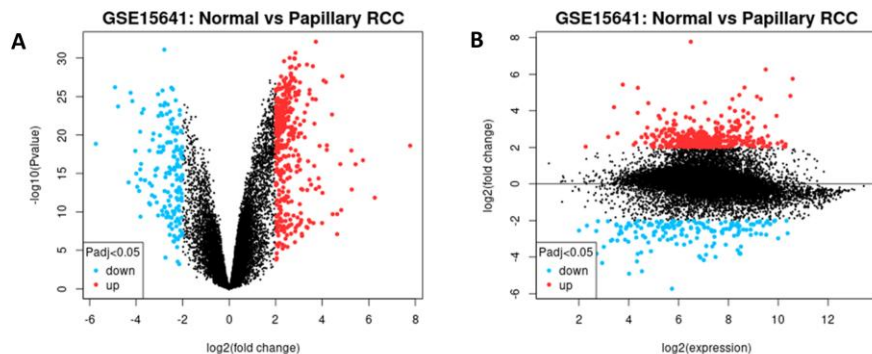


Figure 1. Differential Gene Expression Analysis in Normal Tissue vs. Papillary Renal Cell Carcinoma (RCC) (GSE15641). (A) Volcano plot displaying differentially expressed genes (DEGs) between normal tissue and papillary RCC from dataset GSE15641. The x-axis represents the log₂ fold change, while the y-axis represents the -log₁₀ p-value. A total of 565 DEGs were identified, with 402 upregulated genes (red) and 163 downregulated genes (blue) (Padj < 0.05). (B) Mean-difference (MA) plot illustrating gene expression differences from dataset GSE15641. The x-axis represents log₂-transformed gene expression values, while the y-axis shows the log₂ fold change. Red and blue points indicate significantly upregulated and downregulated genes, respectively, while black points represent non-significant genes.

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Table 1. Pathway Enrichment Analysis of Differentially Expressed Genes Using ShinyGo

Enrichment FDR	nGenes	Pathway Genes	Fold Enrichment	Pathway	Genes
0.022289476	7	75	5.036698	Path:hsa03320 PPAR signaling pathway	FABP1 GK HMGCS2 APOC3 LPL PCK1 ADIPOQ
0.006794312	12	161	4.022208	Path:hsa05206 MicroRNAs in cancer	CDKN2A APC2 EFNA5 ITGB3 MCL1 MET NOTCH1 NOTCH3 TIMP3 RECK TP63 CCND2
0.011720878	14	240	3.147936	Path:hsa04020 Calcium signaling pathway	AGTR1 EGF ERBB4 FGF9 HTR6 ITPR1 MET NTRK2 PDE1A PHKA1 PPP3CC PTGER3 BDKRB2 CAMK2A
0.003205598	20	354	3.048849	Path:hsa04151 PI3K-Akt signaling pathway	LAMC3 COL1A1 CSF1 EFNA5 EGF ERBB4 EREG FGF9 ANGPT1 FASLG ITGA3 ITGB3 MCL1 MET NTRK2 PCK1 PPP2R3A PRLR ITGA8 CCND2
0.011720878	16	294	2.93685	Path:hsa04010 MAPK signaling pathway	CSF1 DUSP9 EFNA5 EGF ELK4 ERBB4 EREG MECOM FGF9 ANGPT1 HSPA2 FASLG MET NTRK2 PAK2 PPP3CC
0.015823092	48	1538	1.684201	Path:hsa01100 Metabolic pathways	AGPAT2 ADH1B CTH CYP2A7 CYP2C19 DDC AKR1C1 ABAT DPY5 ENO1 MECOM ALDOB PLCH1 SIRT5 GATM TPK1 GK GMD5 HADH HMGCS2 ACACB HPD HSD11B2 HSD17B1 ARG2 CYP4F3 ARSB MGAT3 ASS1 ATP6V0A4 PCK1 HAO2 PDE1A PDE3B ENPP1 UPB1 FIGC SMOX CSGALNACT2 CSGALNACT1 MAN1C1 BHMT SORD TYRP1 ELOVL6 CHAC1 AGMAT KMO