**Supplementary information**

**Supplementary Tables**

**Supplementary Table. 1.** Search results from GEO database with the keywords

|  |  |  |
| --- | --- | --- |
| **Keywords used** | **Number of results obtained** | **Datasets observed** |
| ccRCC | 2569 | 49 |
| Clear cell renal cell carcinoma | 11307 | 59 |

**Supplementary Table. 2.** TheccRCC datasets selected for the analysis from GEO database

|  |  |  |  |
| --- | --- | --- | --- |
| **GEO accession number** | **Set number** | **Number samples in ccRCC** | **Number of samples in Control** |
| **GSE71963** | Set1 | 32 | 16 |
| **GSE68417** | Set2 | 29 | 14 |
| **GSE66272** | Set3 | 26 | 27 |
| **GSE76351** | Set4 | 12 | 12 |
| **GSE53757** | Set5 | 72 | 72 |
| **GSE40435** | Set6 | 101 | 101 |
| **GSE46699** | Set7 | 67 | 63 |
| **GSE36895** | Set8 | 29 | 23 |
| **GSE14994** | Set9 | 59 | 11 |
| **GSE15641** | Set10 | 32 | 23 |
| **GSE16449** | Set11 | 52 | 18 |
| **GSE17895** | Set12 | 138 | 22 |

**Supplementary Table. 3.** The top 10 enriched gene ontology terms of the differentially expressed genes (FDR < 0.05) identified from the microarray datasets

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Category** | **Term** | **Count** | **FDR** | **P Value** | **Genes** |
| Cellular components | Collagen-containing extracellular matrix | 22 | 4.14E-14 | 3.37E-10 | COL5A2, SFRP1, VWF, AZGP1, LAMA4, DCN, LGALS1, TGFBI, ANGPTL2, PXDN, TIMP1, LOX, VCAN, ANGPTL4, ENTPD1, SERPINE1, HRG, FGF9, PLG, SERPINA5, KNG1, VEGFA |
| Platelet alpha granule | 11 | 4.97E-13 | 4.00E-10 | VWF, EGF, IGFBP3, TIMP1, SERPINE1, LHFPL2, HRG, PLG, SERPINA5, KNG1, VEGFA |
| Basolateral plasma membrane | 16 | 9.82E-13 | 7.79E-10 | CA9, ATP6V1B1, ABCA1, ANK2, SLC13A3, CAV1, AQP2, ABCA8, PTH1R, SLC2A1, SLC22A6, SLC34A1, HPGD, ENTPD1, UMOD, EPCAM |
| Basal part of cell | 17 | 5.67E-12 | 1.81E-09 | CA9, ATP6V1B1, ABCA1, ANK2, SLC13A3, CAV1, AQP2, ABCA8, PTH1R, SLC2A1, EDN1, SLC22A6, SLC34A1, HPGD, ENTPD1, UMOD, EPCAM |
| Apical part of cell | 21 | 2.71E-11 | 3.07E-09 | DPEP1, ATP6V1B1, MAL, ANK2, CYP4A11, ACP3, VASH1, CAV1, AQP2, PTH1R, SLC2A1, SLC7A9, CLIC5, SLC12A1, SLC12A3, SLC34A1, ATP6V0A4, SCNN1A, UMOD, SLC5A12, EPCAM |
| Apical plasma membrane | 19 | 4.92E-11 | 3.15E-09 | DPEP1, ATP6V1B1, MAL, ANK2, CYP4A11, CAV1, AQP2, PTH1R, SLC2A1, SLC7A9, CLIC5, SLC12A1, SLC12A3, SLC34A1, ATP6V0A4, SCNN1A, UMOD, SLC5A12, EPCAM |
| Basal plasma membrane | 16 | 1.25E-10 | 4.68E-09 | CA9, ATP6V1B1, ABCA1, ANK2, SLC13A3, CAV1, AQP2, ABCA8, PTH1R, SLC2A1, SLC22A6, SLC34A1, HPGD, ENTPD1, UMOD, EPCAM |
| Extracellular matrix | 23 | 4.56E-10 | 5.56E-09 | COL5A2, SFRP1, VWF, AZGP1, LAMA4, DCN, LGALS1, TGFBI, ANGPTL2, PXDN, TIMP1, LOX, VCAN, ANGPTL4, ENTPD1, SERPINE1, FGF1, HRG, FGF9, PLG, SERPINA5, KNG1, VEGFA |
| External encapsulating structure | 23 | 1.11E-09 | 5.89E-09 | COL5A2, SFRP1, VWF, AZGP1, LAMA4, DCN, LGALS1, TGFBI, ANGPTL2, PXDN, TIMP1, LOX, VCAN, ANGPTL4, ENTPD1, SERPINE1, FGF1, HRG, FGF9, PLG, SERPINA5, KNG1, VEGFA |
| Cell surface | 29 | 6.56E-09 | 2.48E-08 | ABCA1, SFRP1, VWF, AZGP1, CAV1, ITGA5, PTGER3, ITGB2, BTN3A2, CD163, LGALS1, ABCG1, SLC12A1, SLC34A1, CXCR4, SCARB1, VCAN, ENTPD1, TSPAN8, SCNN1A, HRG, UMOD, MME, PLG, EPCAM, ENO2, HSPA2, SERPINA5, VEGFA |
| Molecular functions | Carboxylic acid binding | 16 | 1.43E-06 | 1.79E-09 | EGLN3, APOC1, FTCD, PTGER3, DDC, FABP6, FABP7, TYMS, HPGD, ASS1, PYGL, ST8SIA4, PCCA, PLOD2, SERPINA5, PCK1 |
| Signalling receptor binding | 38 | 1.93E-04 | 5.90E-07 | DOCK2, ABCA1, SFRP1, VWF, TCF21, GATA3, LAMA4, GRB14, CAV1, ITGA5, ITGB2, PGF, BTN3A2, EDN1, ADM, TGFBI, PPARGC1A, ANGPTL2, PTPRD, PXDN, EGF, GABARAPL1, TIMP1, NETO2, STC2, ANGPTL4, SERPINE1, TSPAN8, FGF1, HRG, CD70, FGF9, PLCL1, PLG, FYB1, TAP1, KNG1, VEGFA |
| Monosaccharide binding | 8 | 1.93E-04 | 7.23E-07 | EGLN3, HK2, PFKP, LGALS1, FBP1, PYGL, ALDOB, PLOD2 |
| Vitamin binding | 10 | 2.21E-04 | 1.11E-06 | EGLN3, ABAT, CALB1, FTCD, DDC, TYMS, OGDHL, PYGL, PCCA, PLOD2 |
| Ion transmembrane transporter activity | 26 | 2.30E-04 | 1.59E-06 | CYBB, ATP6V1B1, ABCA1, ANK2, AZGP1, NDUFA4L2, SLC13A3, CAV1, AQP2, SLC2A1, SLC7A9, SLC22A6, ABCG1, CLIC5, SLC12A1, SLC12A3, SLC13A1, CLCNKB, SLC34A1, KCNJ1, ATP6V0A4, KCNJ15, KCNK3, SCNN1A, SLC5A12, TAP1 |
| Oxidoreductase activity | 22 | 2.30E-04 | 1.72E-06 | CYBB, EGLN3, FMO1, CYP2J2, CYP4A11, ALDH8A1, NDUFA4L2, CP, ADH6, PXDN, HPD, LOX, SCD, HPGD, DIO1, OGDHL, ALDH4A1, HADH, HSD11B2, PLOD2, HAO2, DCXR |
| Transmembrane transporter activity | 27 | 6.68E-04 | 5.84E-06 | CYBB, ATP6V1B1, ABCA1, ANK2, AZGP1, NDUFA4L2, SLC13A3, CAV1, AQP2, ABCA8, SLC2A1, SLC7A9, SLC22A6, ABCG1, CLIC5, SLC12A1, SLC12A3, SLC13A1, CLCNKB, SLC34A1, KCNJ1, ATP6V0A4, KCNJ15, KCNK3, SCNN1A, SLC5A12, TAP1 |
| Transporter activity | 28 | 1.08E-03 | 1.08E-05 | CYBB, ATP6V1B1, ABCA1, ANK2, AZGP1, NDUFA4L2, SLC13A3, CAV1, AQP2, ABCA8, SLC2A1, SLC7A9, SLC22A6, ABCG1, CLIC5, SLC12A1, SLC12A3, SLC13A1, CLCNKB, SLC34A1, KCNJ1, SCARB1, ATP6V0A4, KCNJ15, KCNK3, SCNN1A, SLC5A12, TAP1 |
| Glycosaminoglycan binding | 11 | 1.41E-03 | 1.59E-05 | SFRP1, DCN, PGF, VCAN, FGF1, HRG, FGF9, TNFAIP6, SERPINA5, KNG1, VEGFA |
| Anion transmembrane transporter activity | 15 | 2.13E-03 | 2.66E-05 | ABCA1, AZGP1, SLC13A3, AQP2, SLC2A1, SLC7A9, SLC22A6, ABCG1, CLIC5, SLC12A1, SLC12A3, SLC13A1, CLCNKB, SLC5A12, TAP1 |
| Biological process | Organic acid metabolic process | 44 | 8.96E-18 | 8.96E-18 | DPEP1, GLYAT, ATP6V1B1, DDIT4, ABAT, FMO1, HK2, CYP2J2, CYP4A11, ALDH8A1, GATM, APOC1, CAV1, FTCD, ACSF2, PFKP, DDC, SLC2A1, EDN1, BHMT, FABP6, ADH6, PPARGC1A, FBP1, SLC34A1, HPD, SCD, HPGD, ASS1, DIO1, OGDHL, UMOD, ALDH4A1, HADH, ALDOB, ALDOC, PCCA, PLOD2, ENO2, G6PC1, HAO2, DCXR, PCK1, PCK2 |
| Carboxylic acid metabolic process | 41 | 2.15E-16 | 2.15E-16 | DPEP1, GLYAT, ATP6V1B1, DDIT4, ABAT, HK2, CYP2J2, CYP4A11, ALDH8A1, GATM, APOC1, CAV1, FTCD, ACSF2, PFKP, DDC, SLC2A1, EDN1, BHMT, FABP6, ADH6, PPARGC1A, FBP1, SLC34A1, HPD, SCD, HPGD, ASS1, DIO1, OGDHL, ALDH4A1, HADH, ALDOB, ALDOC, PCCA, PLOD2, ENO2, HAO2, DCXR, PCK1, PCK2 |
| Oxoacid metabolic process | 41 | 6.38E-16 | 6.38E-16 | DPEP1, GLYAT, ATP6V1B1, DDIT4, ABAT, HK2, CYP2J2, CYP4A11, ALDH8A1, GATM, APOC1, CAV1, FTCD, ACSF2, PFKP, DDC, SLC2A1, EDN1, BHMT, FABP6, ADH6, PPARGC1A, FBP1, SLC34A1, HPD, SCD, HPGD, ASS1, DIO1, OGDHL, ALDH4A1, HADH, ALDOB, ALDOC, PCCA, PLOD2, ENO2, HAO2, DCXR, PCK1, PCK2 |
| Monocarboxylic acid metabolic process | 32 | 4.91E-15 | 4.91E-15 | GLYAT, ATP6V1B1, DDIT4, ABAT, HK2, CYP2J2, CYP4A11, ALDH8A1, GATM, APOC1, CAV1, FTCD, ACSF2, PFKP, EDN1, FABP6, ADH6, PPARGC1A, FBP1, SCD, HPGD, OGDHL, ALDH4A1, HADH, ALDOB, ALDOC, PCCA, ENO2, HAO2, DCXR, PCK1, PCK2 |
| Kidney development | 23 | 2.93E-14 | 2.93E-14 | SFRP1, CALB1, TCF21, CYP4A11, GATA3, DCN, AQP2, PGF, TFAP2B, NPHS2, SLC12A1, HEY1, SLC34A1, CXCR4, KCNJ1, HPGD, VCAN, ASS1, FGF1, UMOD, MME, EPCAM, VEGFA |
| Renal system development | 23 | 6.39E-14 | 6.39E-14 | SFRP1, CALB1, TCF21, CYP4A11, GATA3, DCN, AQP2, PGF, TFAP2B, NPHS2, SLC12A1, HEY1, SLC34A1, CXCR4, KCNJ1, HPGD, VCAN, ASS1, FGF1, UMOD, MME, EPCAM, VEGFA |
| Response to drug | 24 | 1.90E-13 | 1.90E-13 | CA9, CYBB, DPEP1, ABAT, SFRP1, CYP2J2, GATA3, CCND1, DDC, TFAP2B, EDN1, LGALS1, TYMS, PPARGC1A, FBP1, SLC34A1, CXCR4, LOX, ASS1, SERPINE1, KCNK3, UMOD, HADH, HSD11B2 |
| Urogenital system development | 23 | 7.91E-13 | 7.91E-13 | SFRP1, CALB1, TCF21, CYP4A11, GATA3, DCN, AQP2, PGF, TFAP2B, NPHS2, SLC12A1, HEY1, SLC34A1, CXCR4, KCNJ1, HPGD, VCAN, ASS1, FGF1, UMOD, MME, EPCAM, VEGFA |
| Response to lipid | 34 | 2.16E-12 | 2.16E-12 | CA9, CYBB, IL10RA, VIM, DDIT4, ABCA1, FMO1, SFRP1, TCF21, ESRRG, CCND1, CAV1, DCN, PTGER3, EDN1, TYMS, ADM, PPARGC1A, ABCG1, HEY1, STC2, SLC34A1, LOX, SCD, HPGD, SCARB1, ASS1, SERPINE1, SCNN1A, UMOD, HSD11B2, LY86, PCK1, PCK2 |
| Response to hypoxia | 21 | 1.56E-11 | 1.56E-11 | CA9, CYBB, DDIT4, EGLN3, ABAT, SFRP1, HK2, CAV1, PGF, SLC2A1, EDN1, ADM, PPARGC1A, STC2, CXCR4, ANGPTL4, KCNK3, HSD11B2, PLOD2, PCK1, VEGFA |

**Supplementary table. 4.** The top 10 enriched pathway terms of the differentially expressed genes (FDR < 0.05) identified from the microarray datasets

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Category** | **Term** | **Count** | **FDR** | **P Value** | **Genes** |
| Pathways | HIF-1-alpha transcription factor network | 12 | 2.03E-08 | 1.15E-11 | CA9, BHLHE41, EGLN3, HK2, CP, ITGB2, SLC2A1, EDN1, ADM, CXCR4, SERPINE1, VEGFA |
| Glycolysis / Gluconeogenesis | 10 | 3.90E-06 | 2.21E-09 | HK2, PFKP, SLC2A1, FBP1, ALDOB, ALDOC, ENO2, G6PC1, PCK1, PCK2 |
| Glucose metabolism | 10 | 6.46E-05 | 3.66E-08 | HK2, PFKP, PHKA2, FBP1, PYGL, ALDOB, ALDOC, ENO2, PCK1, PCK2 |
| HIF-1 signaling pathway | 10 | 5.40E-04 | 3.06E-07 | CYBB, EGLN3, HK2, SLC2A1, EDN1, EGF, TIMP1, SERPINE1, ENO2, VEGFA |
| Pathways in clear cell renal cell carcinoma | 9 | 1.34E-04 | 8.37E-07 | BHLHE41, HK2, PFKP, SLC2A1, ALDOB, ALDOC, PLOD2, ENO2, VEGFA |
| PPAR signaling pathway | 8 | 1.69E-04 | 1.15E-06 | CYP4A11, HMGCS2, FABP6, FABP7, SCD, ANGPTL4, PCK1, PCK2 |
| Metabolism of carbohydrates | 15 | 2.61E-04 | 2.37E-06 | HK2, PFKP, DCN, SLC2A1, PHKA2, FBP1, VCAN, PYGL, ALDOB, ALDOC, ENO2, G6PC1, DCXR, PCK1, PCK2 |
| Proximal tubule transport | 7 | 5.31E-04 | 5.12E-06 | ATP6V1B1, SLC13A3, SLC2A1, SLC7A9, SLC22A6, SLC34A1, ATP6V0A4 |
| Fructose and mannose metabolism | 5 | 7.49E-04 | 7.67E-06 | HK2, PFKP, FBP1, ALDOB, ALDOC |
| Carbon metabolism | 9 | 7.49E-04 | 8.07E-06 | HK2, PFKP, FBP1, OGDHL, ALDOB, ALDOC, PCCA, ENO2, HAO2 |

**Supplementary Figure captions**

**Supplementary Fig. 1.** The volcano plot of the samples taken for analysis from the data12 datasets selected for this study; red dots represent upregulated genes; blue dots represent downregulated genes and black dots represent unchanged genes

**Supplementary Fig. 2.** In the box plot, the DEGs were identified *via* the LIMMA package with a cut‐off criterion of P <0.05.

**Supplementary Fig. 3.** Construction of common DEGs PPI network. The common DEGs network were constructed using STRING 11.5 and visualized using Cytoscape.

**Supplementary Fig. 4.** Centrality analysis of common DEGs. Density distribution degree centrality (a), betweenness centrality (b), and closeness centrality (c).

**Supplementary Fig. 5.** Correlations among centrality parameters. Degree vs betweenness (a), degree vs closeness(b), betweenness vs closeness (c).

**Supplementary fig. 1**



**Supplementary figure 2**



**Supplementary fig. 3**



**Supplementary fig. 4**

**Supplementary fig. 5**