

Supplementary Tables

Please browse Full Text version to see the data of Supplementary Tables 1 to 4.

Supplementary Table 1. NRF2 binding regions in A549 cells identified using ChIP-Seq.

Supplementary Table 2. Known motifs identified by HOMER motif enrichment analysis software.

Supplementary Table 3. NRF2 binding regions in the promoter region.

Supplementary Table 4. Overlapping genes from an integrated analysis of NRF2 TFBS and downregulated genes in the NRF2-knockdown microarray (FC>1.25).

Supplementary Table 5. KEGG pathways from DAVID analysis of overlapping genes.

| Term | PValue | Genes |
|---|----------|---|
| hsa00860:Porphyrin and chlorophyll metabolism | 2.76E-04 | FTMT, UGT1A6, FECH, HMOX1, BLVRB, FTH1 |
| hsa00980:Metabolism of xenobiotics by cytochrome P450 | 6.79E-04 | AKR1C3, AKR1C2, UGT1A6, EPHX1, AKR1C1, MGST1, ALDH3A1 |
| hsa00030:Pentose phosphate pathway | 9.49E-04 | ALDOA, TALDO1, PGD, PFKP, TKT |
| hsa00480:Glutathione metabolism | 0.001937 | GPX2, GSR, GCLC, PGD, GCLM, MGST1 |
| hsa00051:Fructose and mannose metabolism | 0.003073 | ALDOA, TPI1, AKR1B10, AKR1B1, PFKP |
| hsa00590:Arachidonic acid metabolism | 0.018007 | AKR1C3, GPX2, TBXAS1, CYP4F3, CYP4F2 |
| hsa00010:Glycolysis / Gluconeogenesis | 0.022643 | ALDOA, TPI1, PFKP, ALDH3A2, ALDH3A1 |
| hsa00620:Pyruvate metabolism | 0.034972 | ME1, AKR1B1, ALDH3A2, MDH2 |
| hsa00053:Ascorbate and aldarate metabolism | 0.03692 | UGT1A6, UGDH, ALDH3A2 |
| hsa00040:Pentose and glucuronate interconversions | 0.041055 | UGT1A6, AKR1B1, UGDH |
| hsa00140:Steroid hormone biosynthesis | 0.049758 | AKR1C3, AKR1C2, UGT1A6, AKR1C1 |

Supplementary Table 6. NRF2 TFBS genes clinically correlated with data from TCGA LUAD patients with altered KEAP1.

| Gene | Log Ratio | p-Value | q-Value | Tendency |
|-------------|------------------|----------------|----------------|-----------------|
| AKR1C2 | 6.54 | 5.01E-19 | 1.15E-15 | Over-expressed |
| GPX2 | 5.51 | 4.57E-19 | 1.15E-15 | Over-expressed |
| AKR1C1 | 5.31 | 1.50E-16 | 1.72E-13 | Over-expressed |
| ABCC2 | 3.94 | 1.57E-09 | 2.69E-07 | Over-expressed |
| AKR1C3 | 3.66 | 8.52E-17 | 1.06E-13 | Over-expressed |
| UCHL1 | 2.99 | 9.51E-11 | 2.42E-08 | Over-expressed |
| SLC7A11 | 2.72 | 5.31E-15 | 3.54E-12 | Over-expressed |
| TRIM16L | 2.72 | 1.09E-20 | 7.49E-17 | Over-expressed |
| NQO1 | 2.65 | 1.13E-21 | 1.56E-17 | Over-expressed |
| OSGIN1 | 2.39 | 5.02E-14 | 2.87E-11 | Over-expressed |
| SRXN1 | 2.37 | 3.68E-16 | 3.89E-13 | Over-expressed |
| CYP24A1 | 2.14 | 3.99E-05 | 4.71E-04 | Over-expressed |
| TXNRD1 | 2.09 | 2.45E-13 | 1.24E-10 | Over-expressed |
| PIR | 2.02 | 5.52E-20 | 2.53E-16 | Over-expressed |
| UGDH | 1.96 | 1.95E-18 | 3.82E-15 | Over-expressed |
| CES1 | 1.95 | 1.48E-04 | 1.29E-03 | Over-expressed |
| KYNU | 1.89 | 6.88E-06 | 1.25E-04 | Over-expressed |
| NEIL3 | 1.82 | 1.89E-07 | 8.79E-06 | Over-expressed |
| GCLC | 1.81 | 2.17E-08 | 1.90E-06 | Over-expressed |
| RSPO3 | 1.73 | 4.99E-04 | 3.22E-03 | Over-expressed |
| CARD14 | 1.7 | 4.32E-08 | 3.04E-06 | Over-expressed |
| PGD | 1.68 | 9.21E-18 | 1.40E-14 | Over-expressed |
| ABCB6 | 1.66 | 7.94E-16 | 7.27E-13 | Over-expressed |
| PTGR1 | 1.63 | 1.21E-13 | 6.39E-11 | Over-expressed |
| GCLM | 1.59 | 1.37E-15 | 1.10E-12 | Over-expressed |
| GSR | 1.55 | 2.24E-18 | 3.85E-15 | Over-expressed |

Supplementary Table 7. KEGG pathways from DAVID analysis of NRF2 TFBS genes.

| Term | PValue | Genes |
|---|----------|---|
| hsa00860:Porphyrin and chlorophyll metabolism | 0.010765 | FTMT, UGT1A6, FECH, HMOX1, CPOX, BLVRB, CP, FTH1, EARS2 |
| hsa04510:Focal adhesion | 0.015366 | CAV2, TLN2, PDGFA, ITGB4, ITGB1, PTEN, SRC, CTNNB1, SHC1, PIK3R1, SPP1, PRKCA, COL4A4, ACTN4, ACTN1, MAPK10, HGF, FLNC, COL5A3, CAPN2, PPP1CB, FLNB, COL5A1, COL4A6, SPDYA, LAMA2, VEGFC, LAMA3, CCND3, MAPK8, LAMC1 |
| hsa00010:Glycolysis/Gluconeogenesis | 0.025179 | ALDOA, GPI, TPI1, G6PC, LDHAL6B, DLD, PFKP, ADH7, GAPDH, ALDH3A2, ALDH3A1, ENO1 |
| hsa00030:Pentose phosphate pathway | 0.02736 | ALDOA, GPI, TALDO1, PGD, PFKP, TKT, LOC729020 |
| hsa05200:Pathways in cancer | 0.028938 | BID, FGFR2, PTGS2, PDGFA, EGLN3, NFKBIA, NFKB1, GLI2, ITGB1, TCF7L2, PTEN, CTNNB1, TGFA, RARA, FGF1, MYC, PIK3R1, CEBPA, COL4A4, PRKCA, AR, HSP90AA1, CTBP2, TGFB2, SMAD3, CDK6, MAPK10, HGF, MECOM, COL4A6, FZD7, CTNNA3, LAMA2, VEGFC, CBLB, FZD10, LAMA3, HIF1A, PLCG1, IKBKG, MAPK8, LAMC1, GSTP1 |
| hsa04520:Adherens junction | 0.029617 | PTPRB, PTPRJ, PARD3, WASF3, ACTN4, TGFB2, SMAD3, ACTN1, FER, TCF7L2, CTNNA3, SRC, CTNNB1, TJP1 |
| hsa00620:Pyruvate metabolism | 0.033025 | ME1, LDHAL6B, AKR1B1, DLD, ACYP2, ACACB, ALDH3A2, MDH2, PC |
| hsa04012:ErbB signaling pathway | 0.035574 | PRKCA, NRG3, BTC, MAPK10, SRC, CBLB, PLCG1, EREG, CAMK2D, TGFA, SHC1, MAPK8, MYC, ABL2, PIK3R1 |
| hsa00051:Fructose and mannose metabolism | 0.038929 | MTMR2, ALDOA, TPI1, AKR1B15, MPI, PFKFB3, AKR1B10, AKR1B1, PFKP |

Supplementary Table 8. Primers used for qRT-PCR analysis.

| | | |
|---------|---------|------------------------------|
| CAPN2 | Forward | 5'-GAGTTGAAGAAGCCCCCTCC-3' |
| | Reverse | 5'-GCTAGATTCGGACGGGAGTG-3' |
| LAMC1 | Forward | 5'-CACTGTAGTCCTGTGGGCTC-3' |
| | Reverse | 5'-GTAAGCCAGGAGTGATGGGG-3' |
| MAPK8 | Forward | 5'-TGAAGCAGAAGCTCCACCAC-3' |
| | Reverse | 5'-CAGCCCTCTCCTTTAGGTGC-3' |
| SHC1 | Forward | 5'-ACTTGGGAGCTACATTGCCTG-3' |
| | Reverse | 5'-GCAAACAGATGCCACCTCCA-3' |
| SPDYA | Forward | 5'-CTTCCGCAGTCCTTCCTCAG-3' |
| | Reverse | 5'-GATGTGTTGTGAGACACCACC-3' |
| SPP1 | Forward | 5'-AAATACCCAGATGCTGTGGC-3' |
| | Reverse | 5'-CCCACAGACCCTTCCAAGTAAG-3' |
| AKR1B10 | Forward | 5'-TGTGGGCCTGGGCACTTGGA-3' |
| | Reverse | 5'-GGTCCTCCCGCTTCACAGCC-3' |