SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure 1.

A) Volcano plot of differentially expressed genes from Pan Cancer Pathway panel of 11 ccRCC tumor samples when comparing PDK2/PDK3 positive versus PDK2/PDK3 negative tumors. B) Volcano plot of differentially expressed genes from Immune Exhaustion panel of 18 ccRCC tumor samples when comparing PDK2/PDK3 positive versus PDK2/PDK3 negative tumor.

Supplementary Figure 2.

In silico validation of correlation analysis of differentially expressed genes in PDK2 and PDK3 high tumors from nCounter Pan Cancer Panel. Correlation analysis of PDK2 and PDK3 mRNA expression with FN1 (A), MMP7 (B), COL1A1 (C) and EPOR (D) mRNA expression is shown. Data are from KIRC, TCGA.

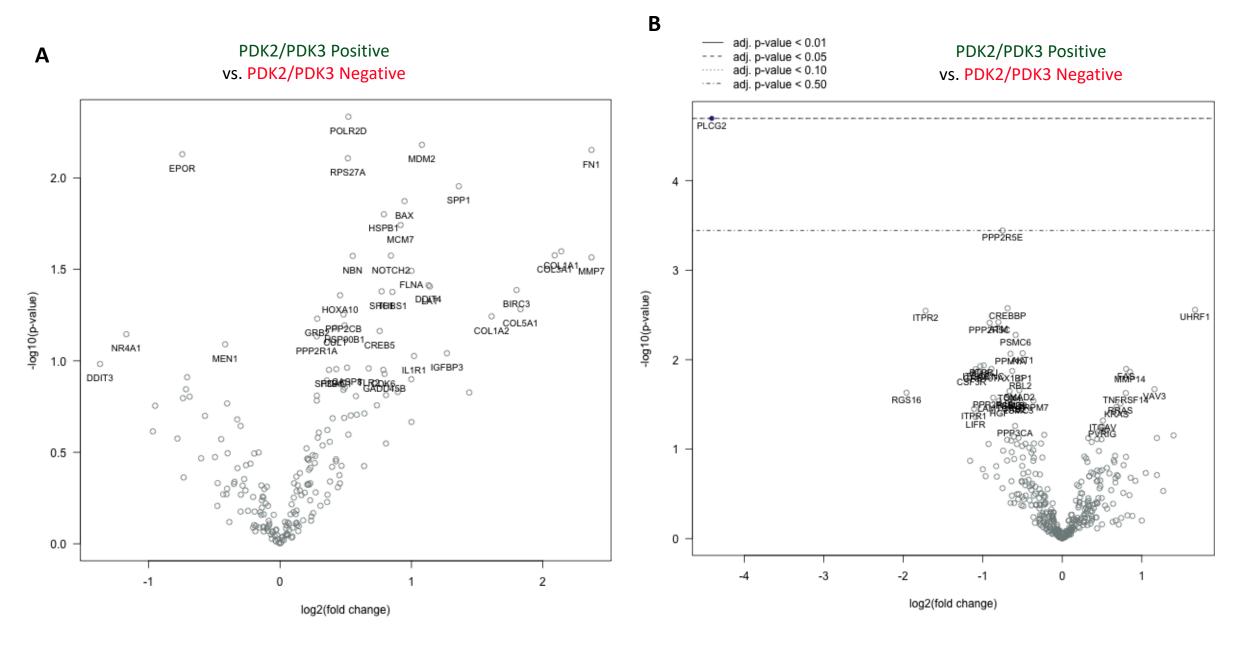
Supplementary Figure 3.

In silico validation of correlation analysis of differentially expressed genes in PDK2 and PDK3 high tumors from nCounter Immune Exhaustion Panel. Correlation analysis of PDK2 and PDK3 mRNA expression with UHRF1 (A), VAV3 (B), RGS16 (C) and PLCG2 (D) mRNA expression is shown. Data are from KIRC, TCGA.

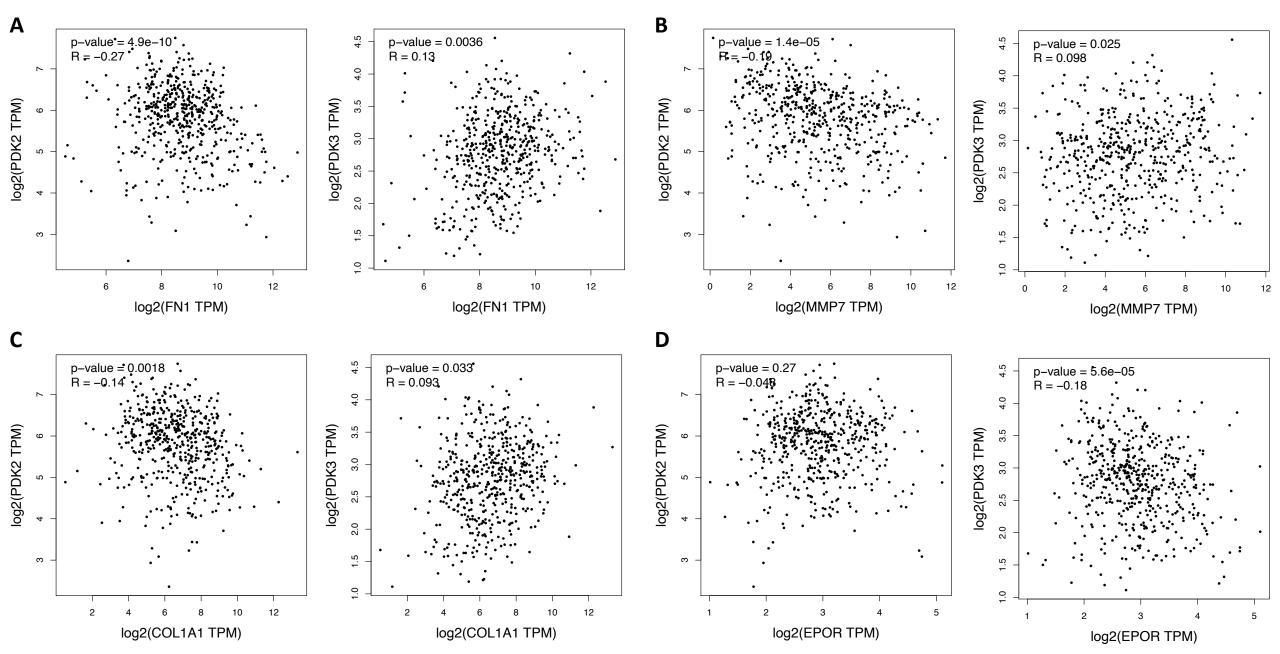
Supplementary Figure 4.

Correlation analysis of PDK1-4 mRN expression with HIF1 α (*HIF1A*) (A) and HIF2 α (*EPAS1*) (B) mRNA expression. Data are from KIRC, TCGA.

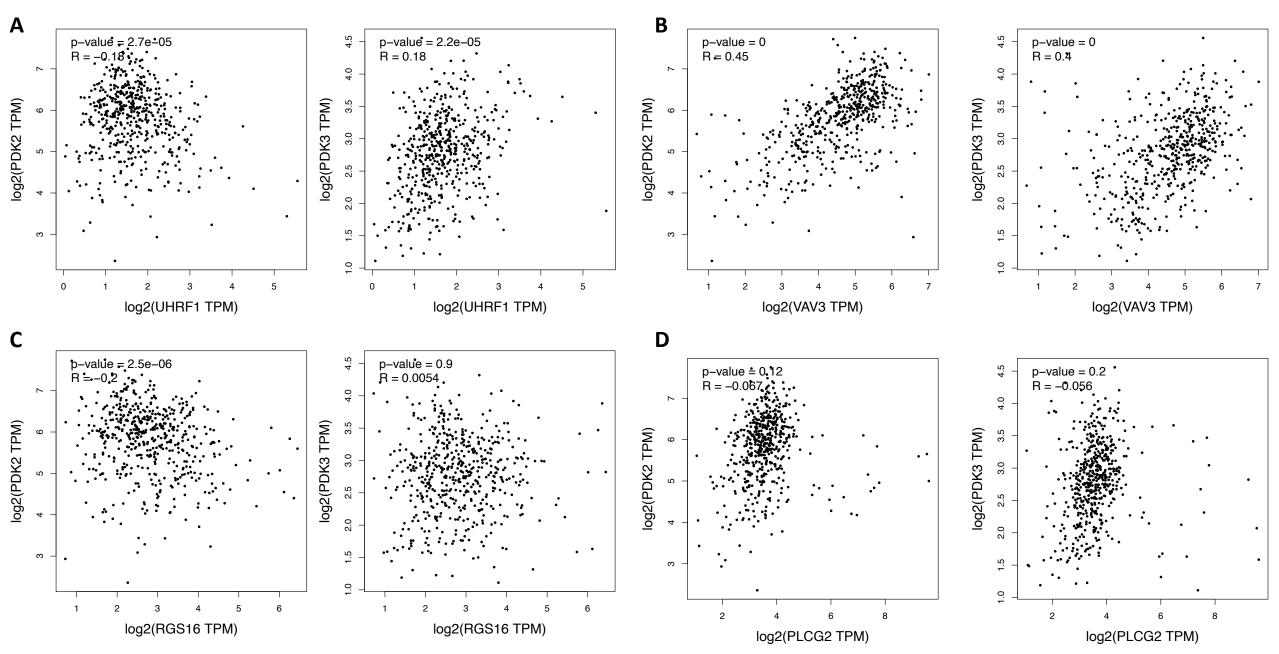
Supplementary Figure 1.



Supplementary Figure 2.



Supplementary Figure 3.



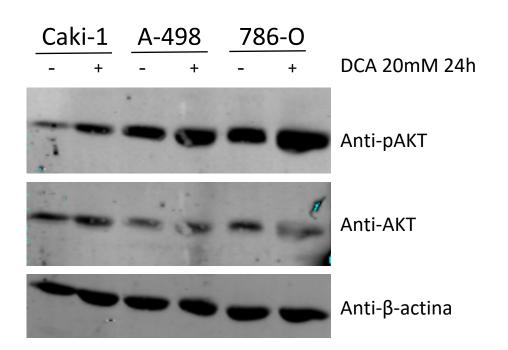
SUPPLEMENTARY TABLE 1. Differentilly Expressed Genes in PDK2/PDK3 positive versus PDK2/PDK3 negative tumors in nCounter PanCancer Pathway Panel

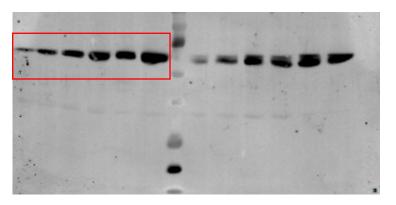
| | Log2 fold | std error | Lower | Upper | Linear fold | Lower | Upper | P-value |
|-------------|-----------|-----------|------------|------------|-------------|------------|------------|---------|
| | change | (log2) | confidence | confidence | change | confidence | confidence | |
| FN1-mRNA | 2.37 | 0.683 | 1.03 | 3.71 | 5.17 | 2.05 | 13.1 | 0.00703 |
| MMP7-mRNA | 2.37 | 0.9 | 0.607 | 4.13 | 5.17 | 1.52 | 17.6 | 0.0272 |
| COL1A1-mRNA | 2.14 | 0.799 | 0.575 | 3.71 | 4.41 | 1.49 | 13.1 | 0.0252 |
| COL3A1-mRNA | 2.09 | 0.787 | 0.543 | 3.63 | 4.24 | 1.46 | 12.4 | 0.0265 |
| BIRC3-mRNA | 1.8 | 0.757 | 0.32 | 3.29 | 3.49 | 1.25 | 9.77 | 0.041 |
| SPP1-mRNA | 1.36 | 0.427 | 0.524 | 2.2 | 2.57 | 1.44 | 4.59 | 0.0111 |
| LAT-mRNA | 1.14 | 0.475 | 0.214 | 2.07 | 2.21 | 1.16 | 4.21 | 0.0392 |
| DDIT4-mRNA | 1.13 | 0.467 | 0.215 | 2.05 | 2.19 | 1.16 | 4.13 | 0.0386 |
| MDM2-mRNA | 1.08 | 0.306 | 0.476 | 1.68 | 2.11 | 1.39 | 3.2 | 0.00659 |
| BAX-mRNA | 0.947 | 0.308 | 0.342 | 1.55 | 1.93 | 1.27 | 2.93 | 0.0134 |
| MCM7-mRNA | 0.917 | 0.318 | 0.294 | 1.54 | 1.89 | 1.23 | 2.91 | 0.0181 |
| THBS1-mRNA | 0.855 | 0.361 | 0.148 | 1.56 | 1.81 | 1.11 | 2.95 | 0.042 |
| NOTCH2-mRNA | 0.844 | 0.319 | 0.219 | 1.47 | 1.8 | 1.16 | 2.77 | 0.0266 |
| HSPB1-mRNA | 0.79 | 0.266 | 0.268 | 1.31 | 1.73 | 1.2 | 2.48 | 0.0158 |
| SHC1-mRNA | 0.773 | 0.326 | 0.135 | 1.41 | 1.71 | 1.1 | 2.66 | 0.0417 |
| NBN-mRNA | 0.553 | 0.209 | 0.143 | 0.963 | 1.47 | 1.1 | 1.95 | 0.0267 |
| POLR2D-mRNA | 0.52 | 0.139 | 0.247 | 0.793 | 1.43 | 1.19 | 1.73 | 0.00463 |
| RPS27A-mRNA | 0.516 | 0.152 | 0.219 | 0.814 | 1.43 | 1.16 | 1.76 | 0.00781 |
| HOXA10-mRNA | 0.457 | 0.195 | 0.0748 | 0.84 | 1.37 | 1.05 | 1.79 | 0.0438 |
| FLNA-mRNA | 1 | 0.397 | 0.227 | 1.78 | 2.01 | 1.17 | 3.44 | 0.0322 |
| EPOR-mRNA | -0.744 | 0.216 | -1.17 | -0.32 | 0.597 | 0.445 | 0.801 | 0.00742 |

SUPPLEMENTARY TABLE 2. Differentilly Expressed Genes in PDK2/PDK3 positive versus PDK2/PDK3 negative tumors in nCounter Immune Exhaustion Panel

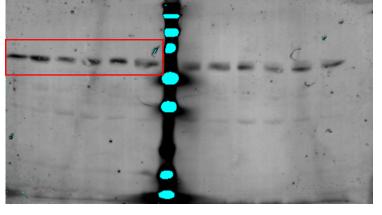
| | 1 0 | -4-1 | | 11 | 1 ! | | 11 | D |
|---------------|--------------|---------------------|--------|------------------|-------------|------------------|------------------|----------|
| , | Log2 fold | std error (log2) | | Upper confidence | Linear fold | Lower confidence | Upper confidence | P-value |
| UHRF1-mRNA | 1.67 | 0.474 | 0.744 | 2.6 | 3.19 | 1.68 | 6.07 | 0.00277 |
| VAV3-mRNA | 1.16 | 0.455 | 0.269 | 2.05 | 2.24 | 1.2 | 4.15 | 0.0214 |
| MMP14-mRNA | 0.851 | 0.307 | 0.249 | 1.45 | 1.8 | 1.19 | 2.74 | 0.0137 |
| FAS-mRNA | 0.803 | 0.286 | 0.242 | 1.36 | 1.74 | 1.18 | 2.57 | 0.0127 |
| TNFRSF14-mRN/ | 0.799 | 0.32 | 0.173 | 1.43 | 1.74 | 1.13 | 2.69 | 0.0236 |
| RRAS-mRNA | 0.732 | 0.309 | 0.126 | 1.34 | 1.66 | 1.09 | 2.53 | 0.0309 |
| KRAS-mRNA | 0.683 | 0.294 | 0.106 | 1.26 | 1.61 | 1.08 | 2.4 | 0.0338 |
| ITGAV-mRNA | 0.511 | 0.239 | 0.0431 | 0.978 | 1.42 | 1.03 | 1.97 | 0.048 |
| TRPM7-mRNA | -0.364 | 0.152 | -0.661 | -0.0669 | 0.777 | 0.632 | 0.955 | 0.0288 |
| AKT1-mRNA | -0.499 | 0.166 | -0.825 | -0.173 | 0.708 | 0.564 | 0.887 | 0.00848 |
| SMC3-mRNA | -0.518 | 0.218 | -0.946 | -0.0901 | 0.698 | 0.519 | 0.939 | 0.0305 |
| RBL2-mRNA | -0.526 | 0.196 | -0.91 | -0.143 | 0.694 | 0.532 | 0.906 | 0.0162 |
| SMAD2-mRNA | -0.541 | 0.213 | -0.96 | -0.123 | 0.687 | 0.514 | 0.918 | 0.022 |
| PSMC6-mRNA | -0.587 | 0.182 | -0.944 | -0.23 | 0.666 | 0.52 | 0.852 | 0.00529 |
| TAB2-mRNA | -0.601 | 0.252 | -1.09 | -0.108 | 0.659 | 0.468 | 0.928 | 0.0296 |
| CBLB-mRNA | -0.618 | 0.254 | -1.12 | -0.119 | 0.652 | 0.461 | 0.921 | 0.0274 |
| TAX1BP1-mRNA | -0.63 | 0.227 | -1.07 | -0.186 | 0.646 | 0.475 | 0.879 | 0.0134 |
| PSMD6-mRNA | -0.639 | 0.262 | -1.15 | -0.125 | 0.642 | 0.449 | 0.917 | 0.0269 |
| PPM1A-mRNA | -0.652 | 0.218 | -1.08 | -0.225 | 0.636 | 0.473 | 0.856 | 0.00859 |
| TOX4-mRNA | -0.664 | 0.263 | -1.18 | -0.148 | 0.631 | 0.442 | 0.902 | 0.0225 |
| CREBBP-mRNA | -0.689 | 0.194 | -1.07 | -0.309 | 0.62 | 0.477 | 0.807 | 0.00266 |
| PPP2R5E-mRNA | -0.752 | 0.167 | -1.08 | -0.425 | 0.594 | 0.473 | 0.745 | 0.00036 |
| HGF-mRNA | -0.794 | 0.339 | -1.46 | -0.128 | 0.577 | 0.364 | 0.915 | 0.0327 |
| LAMTOR3-mRNA | -0.797 | 0.332 | -1.45 | -0.146 | 0.575 | 0.366 | 0.904 | 0.0289 |
| ATM-mRNA | -0.804 | 0.238 | -1.27 | -0.338 | 0.573 | 0.414 | 0.791 | 0.00381 |
| PPP2R1B-mRNA | -0.869 | 0.356 | -1.57 | -0.171 | 0.548 | 0.338 | 0.888 | 0.0266 |
| CCNC-mRNA | -0.892 | 0.318 | -1.52 | -0.269 | 0.539 | 0.35 | 0.83 | 0.0127 |
| PPP2R5C-mRNA | -0.915 | 0.271 | -1.45 | -0.383 | 0.531 | 0.367 | 0.767 | 0.00387 |
| PTPRJ-mRNA | -0.988 | 0.347 | -1.67 | -0.308 | 0.504 | 0.315 | 0.808 | 0.0116 |
| IL18-mRNA | -1.03 | 0.361 | -1.73 | -0.318 | 0.491 | 0.301 | 0.802 | 0.0118 |
| GRB10-mRNA | -1.06 | 0.382 | -1.81 | -0.312 | 0.479 | 0.285 | 0.805 | 0.0135 |
| ITGA6-mRNA | -1.09 | 0.39 | -1.86 | -0.328 | 0.469 | 0.276 | 0.797 | 0.0128 |
| LIFR-mRNA | -1.09 | 0.498 | -2.06 | -0.114 | 0.47 | 0.239 | 0.924 | 0.0438 |
| ITPR1-mRNA | -1.11 | 0.485 | -2.06 | -0.163 | 0.462 | 0.239 | 0.893 | 0.0355 |
| CSF3R-mRNA | -1.14 | 0.418 | -1.96 | -0.325 | 0.452 | 0.256 | 0.798 | 0.0146 |
| ITPR2-mRNA | -1.72 | 0.49 | -2.68 | -0.763 | 0.303 | 0.156 | 0.589 | 0.00285 |
| RGS16-mRNA | -1.96 | 0.782 | -3.49 | -0.427 | 0.257 | 0.0888 | 0.744 | 0.0234 |
| PLCG2-mRNA | -4.41 | 0.74 | -5.86 | -2.96 | 0.0471 | 0.0172 | 0.129 | 2.01e-05 |

Full blots, uncropped from FIGURE 5A

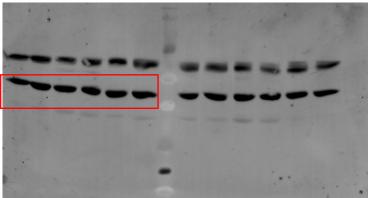




Anti-pAKT



Anti-AKT



Anti- β -actina