

Supplementary Table 1 - Reagents list

| Antibodies | | | | | |
|--------------------------------------|-------------|-------------------|------------|---------------|---|
| Protein | Application | Supplier | Catalog # | Concentration | Additional notes |
| Cleaved PARP | WB | Cell Signaling | 9544 | 1:1000 | |
| p-AMPK (Thr172) | WB | Cell Signaling | 2535 | 1:1000 | |
| AMPK α | WB | Cell Signaling | 5831 | 1:1000 | |
| GAPDH | WB | Sigma | G8795 | 1:5000 | |
| p-Her2 (Tyr1221/1222) | WB | Cell Signaling | 2243 | 1:1000 | |
| Her2 | WB | Cell Signaling | 4290 | 1:1000 | |
| p-ERK1/2 (Thr202/Tyr204) | WB | Cell Signaling | 9106 | 1:2000 | |
| ERK1/2 | WB | Cell Signaling | 9102 | 1:1000 | |
| p-Akt (Ser473) | WB | Cell Signaling | 4060 | 1:1000 | |
| Akt | WB | Cell Signaling | 9272 | 1:1000 | |
| p-PRAS40 (Ser246) | WB | Cell Signaling | 13175 | 1:1000 | |
| p-GSK-3 β (Ser9) | WB | Cell Signaling | 5558 | 1:1000 | |
| p-S6-RP (Ser240/244) | WB | Cell Signaling | 5364 | 1:2000 | |
| α -Tubulin | WB | Santa Cruz | 8035 | 1:2000 | Used for all except Figs. S1C, 4B, 5B, 6G |
| α -Tubulin | WB | Cell Signaling | 3873 | 1:5000 | Used for Figs. S1C, 4B, 5B, 6G |
| p-PDH | WB | Calbiochem | AP10062 | 1:10000 | |
| NRF2 | WB | Cell Signaling | 12721 | 1:1000 | |
| NQO1 | WB | Cell Signaling | 62262 | 1:1000 | |
| KEAP1 | WB | Proteintech | 10503-2-AP | 1:1000 | |
| Snail | WB | Cell Signaling | 3879 | 1:1000 | |
| Her2 | IF | Cell Signaling | 2165 | 1:200 | |
| Cleaved Caspase-3 (Asp175) | IF | Cell Signaling | 9661 | 1:300 | |
| Ki67 - AlexaFluor 488 | IF | BD Pharmingen | 561165 | 1:100 | |
| NRF2 | IF | GeneTex | GTX103322 | 1:250 | |
| Annexin V - AlexaFluor 488 | Flow | Life Technologies | V13245 | 1:20 | |
| Goat anti-rabbit AlexaFluor 488 | IF | Life Technologies | A11034 | 1:5000 | |
| Goat anti-rabbit AlexaFluor 568 | IF | Life Technologies | A11036 | 1:5000 | |
| Goat anti-rabbit AlexaFluor 680 | WB | Life Technologies | A21076 | 1:5000 | |
| Goat anti-rabbit IRDye® 800CW | WB | LiCor | 925-32211 | 1:5000 | |
| Goat anti-mouse IRDye® 800CW | WB | LiCor | 926-32210 | 1:5000 | |
| Anti-rabbit IgG, HRP-linked antibody | WB | Cell Signaling | 7074P2 | 1:5000 | |
| Ki67 | IHC | Thermo Scientific | RM-9106-S | | |

| Other dyes and staining materials | | | | | |
|-----------------------------------|-------------|----------------|-----------|---------------|----------------------------------|
| Compound | Application | Supplier | Catalog # | Concentration | Additional Notes |
| BODIPY 493/503 | IF | Thermo | D3922 | | |
| Hoechst 33342 | IF | Thermo | H1399 | 2 μ g/mL | |
| DCFDA | IF, Flow | Abeam | ab113851 | 10 μ M | |
| mitoSOX Red | Flow | Thermo | M36008 | 2.5 μ M | |
| Prolong Gold with DAPI | IF | Cell Signaling | 8961 | | Used for all images with DAPI |
| Prolong Gold | IF | Thermo | P36930 | | Used for all images with Hoechst |

| Taqman gene expression probes | | | |
|-------------------------------|-----------------------------|---------------|------------------|
| Taqman Master mix | Applied Biosystems #4369016 | | |
| Gene | Species | Catalog # | Additional notes |
| Actb | mouse | Mm02619580_g1 | |
| Gapdh | mouse | Mm99999915_g1 | Used for Fig 6E |
| Cpt1a | mouse | Mm01231183_m1 | |
| Cpt1b | mouse | Mm00487191_g1 | |
| Gclm | mouse | Mm01324400_m1 | |
| Nqo1 | mouse | Mm01253561_m1 | |
| Hmox1 | mouse | Mm00516005_m1 | |
| Slc7a11 | mouse | Mm00442530_m1 | |
| NRF2 (Nfe2l2) | mouse | Mm00477784_m1 | |
| Pgd | mouse | Mm00503037_m1 | |
| Txnrd1 | mouse | Mm00443675_m1 | |

| SYBR green gene expression primers | | | |
|------------------------------------|-------------------------|--------------------------|------------------|
| SYBR green master mix | Bio-Rad #172-5121 | | |
| Gene | Forward sequence | Reverse Sequence | Additional notes |
| CD36 | GAACCACTGCTTCAAAAAGCTGG | TGCTGTTCTTTGCCACGTC | |
| Actb | CATGAAGATCCTGACCGAGCGTG | TCTGCTGGAAGGTGGACAGTGAGG | |
| Nqo1 | TATCCTCCGAGTCATCTCTAGCA | TCTGAGCTTCCAGCTTCTTG | Used for Fig S3A |
| Hmox1 | CAGGTGATGCTGACAGAGGA | GAGAGTGAGGACCCACTGGA | Used for Fig S3A |
| Gclm | GCCACCAGATTGACTGCCITTTG | TGCTCTTACAGTACCGAGTACC | Used for Fig S3A |

| CRISPR Screen Library Preparation Primers | | | |
|--|--|---|--|
| DNA Polymerase Hot Start Version | Takara #R007B | | |
| PCR1 | Forward Sequence | Reverse Sequence | |
| | aatggactatcatatgcttaccgtaactgaagtatttcg | ggaaagaatagtagacataatagcaacagacatacaactaaag | |
| PCR2 | Forward Sequence | | |
| | Illumina P5 and Illumina seq | | |
| | AAATGATACGGCGACCACCGAGATCTACACTCTTTCCCTACACGACGCTCTTCCGATCT – 2-5bp stagger sequence | | |
| | Reverse Sequence | | |
| Illumina P7 – 8bp barcode sequence – Illumina seq R – 1-9bp stagger sequence – priming site | | | |
| CAAGCAGAAGACGGCATACGAGAT – 8bp barcode – GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCT – stagger sequence – TCTACTATTCCTTTCCCTGCAGTGT | | | |

caNRF2 Cloning Primers**Forward sequence**

acttgtcagcggccaccatggattacaaagacgatgacgataaggccacgacatccagacagaccagtgg

Reverse sequence

atcagcggcccgactagttttcttctgtatctggtcttctgc

Cell culture reagents

| Compound | Supplier | Catalog # | Concentration | Additional notes |
|-----------------------------------|--------------------------------------|-----------|---------------|---|
| RPMI-1640 | Sigma | R8758 | | |
| DMEM | Corning | 10-017-CV | | |
| Pen/Strep | Gibco | 15140-122 | 1x | |
| L-Glutamine | Gibco | 25030-081 | 2mM | |
| Fetal Bovine Serum (FBS) | Corning | 35-010-CV | | |
| Super Calf Serum (SCS) | Gemini | 100-510 | | |
| EGF | Sigma | E4127 | 10ng/mL | |
| bFGF | Invitrogen | 13256-029 | 20ng/mL | |
| B27 Supplement | Invitrogen | 17504-044 | 1x | |
| Poly(2-hydroxyethyl methacrylate) | Sigma | P3932 | | |
| Doxycycline | RPI | D43020 | 2µg/mL | |
| Insulin | Sigma | I6634 | 5µg/mL | |
| Prolactin | National hormone and peptide program | | 5µg/mL | Provided by A. F. Parlow (Harbor-UCLA Medical Center) |
| hydrocortisone | Sigma | H0396 | 1µg/mL | |
| Progesterone | Sigma | P7556 | 1µM | |

Cell treatment compounds

| Compound | Supplier | catalog # | Additional Notes |
|----------------------------------|-----------------|-------------|------------------|
| Lapatinib | Selleckchem | S1028 | |
| N-acetyl cysteine (NAC) | Sigma | A9165 | |
| Glutathione | Sigma | G6013 | |
| Etomoxir | Tocris | 4539 | |
| 6-Aminonicotinamide | Cayman Chemical | 10009315 | |
| DHEA | Sigma | D4000 | |
| TBHP | Abcam | ab113851 | From DCFDA kit |
| TBHQ | Sigma | 112941 | |
| BPTES | Sigma | SML0601-5MG | |
| CB-839 | Cayman | 22038 | |
| dimethyl α -ketoglutarate | Sigma | 349631 | |
| MG-132 | Sigma | M7449-200UL | |

Supplementary Table 2 - NRF2 gene signatures

| NRF2 Core Gene Signature | |
|---------------------------------|--------------|
| Gene name | Notes |
| ABCB6 | |
| ABCC1 | |
| ABCC2 | |
| ABCG2 | |
| ABHD4 | |
| ADAM23 | |
| AKR1B10 | |
| AKR1C1 | |
| AKR1C3 | |
| ALDH3A1 | |
| ALDH3A2 | |
| ASF1A | |
| ASNS | |
| ASPH | |
| BLVRB | |
| C14ORF149 | 1 |
| C16ORF28 | 1,2 |
| C1S | |
| CAMKK1 | 1 |
| CBR1 | |
| CBR3 | |
| CCDC77 | 1 |
| CCND3 | |
| CDKN2B | |
| CES1 | |
| CLN5 | |
| CPLX2 | |
| CXCR7 | |
| CYP4F11 | |
| DDC | |
| DEGS1 | |
| DGKG | |
| DKFZP762E1312 | 1,2 |
| DOCK10 | |
| EPHX1 | |
| F2RL2 | |
| FAM55C | |
| FTH1 | |
| FZD7 | |
| G6PD | |
| GALNT13 | 1 |

| NRF2 18-gene Signature |
|-------------------------------|
| Gene name |
| FTH1 |
| G6PD |
| GCLC |
| GCLM |
| GPX2 |
| GSR |
| HMOX1 |
| HMOX2 |
| IDH1 |
| ME1 |
| NQO1 |
| NQO2 |
| PGD |
| PRDX1 |
| SLC7A11 |
| TXN |
| TXN2 |
| TXNRD1 |

| | |
|-----------|-----|
| GCLC | |
| GCLM | |
| GLA | |
| GPC1 | |
| GPX2 | |
| GSR | |
| HGD | |
| HMOX1 | |
| HRB | 1,2 |
| HSPA1B | |
| HTATIP2 | |
| IDH1 | |
| KIAA0319 | |
| LOC642252 | 1,2 |
| LOC644799 | 1,2 |
| LRP12 | |
| LRP8 | |
| LTB4DH | 1,2 |
| MAFG | |
| MAP2 | |
| MARS | |
| MCM10 | |
| ME1 | |
| MEGF9 | |
| MGT1 | 1 |
| MSC | |
| NCF2 | |
| NEIL3 | |
| NFE2L2 | |
| NLN | 1 |
| NQO1 | |
| NQO2 | |
| NR0B1 | 2 |
| NRCAM | |
| OSGIN1 | |
| P2RY6 | |
| PA2G4 | |
| PBEF1 | 1,2 |
| PCK2 | |
| PGD | |
| PIR | |
| POPDC3 | |
| PPAT | |
| PRDX1 | |
| RRM2 | |

| | |
|----------|-----|
| SERPINE1 | |
| SFN | |
| SLC38A6 | |
| SLC6A6 | |
| SLC7A11 | |
| SORD | |
| SPANXA1 | 1,2 |
| SPANXB1 | 1,2 |
| SPP1 | |
| SQSTM1 | |
| SRXN1 | 1 |
| TALDO1 | |
| TFRC | |
| TGFB2 | |
| TKT | |
| TM4SF20 | 2 |
| TRIM16 | |
| TSPAN7 | |
| TXN | |
| TXNRD1 | |
| UCHL1 | |
| UIP1 | 1,2 |

From Romero, R. et al. Keap1 loss promotes Kras-driven lung cancer and results in dependence on glutaminolysis. *Nat Med* 23, 1362-1368 (2017).

1: Gene excluded from survival analysis (not found in human gene expression datasets).

2: Gene excluded from GSEA (not found in human recurrent tumor gene expression datasets).