**Supplementary File 5A. Summary of transcriptome analysis of LNCaP cells treated with GCN2iB.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Treatment** | **Time (hours)** | **Number of Transcriptsa,b** | | | | | |
| **Increase** | **≥ 2X Increase** | **Decrease** | **≥ 2X Increase** | **Total** | **≥ 2X Total** |
| GCN2iB | 6 | 2075 | 2 | 1454 | 25 | 3529 | 27 |
| GCN2iB | 24 | 4205 | 253 | 3738 | 391 | 7943 | 644 |

aUnique Ensemble transcript IDs

bFalse discovery rate (fdr), Benjamini-Hochberg adjusted *p*-value ≤ 0.05

**Supplementary File 5B. siRNAs used in PCa growth studies.**

|  |  |  |  |
| --- | --- | --- | --- |
| **siRNA Name** | **siRNA Sequencea** | **Vendor** | **Catalog Number** |
| Non-Targeting Control | UGGUUUACAUGUCGACUAA | Dharmacon | D-001810-10-20 |
|  | UGGUUUACAUGUUGUGUGA | Dharmacon |  |
|  | UGGUUUACAUGUUUUCUGA | Dharmacon |  |
|  | UGGUUUACAUGUUUUCCUUA | Dharmacon |  |
| Non-Targeting Control | UGGUUUACAUGUCGACUAA | Dharmacon | D-001910-10-05 |
|  | UGGUUUACAUGUUUUCUGA | Dharmacon |  |
|  | UGGUUUACAUGUUUUCCUA | Dharmacon |  |
|  | UCCUUUACAUGUUGUGUGA | Dharmacon |  |
| HRI-1 | gcacaaacUUcacgUUacU | Dharmacon | J-005007-05 |
| HRI-2 | gaUUaagggUgcaacUaaa | Dharmacon | J-005007-06 |
| HRI-3 | gcagaaaUccaggUgUUaa | Dharmacon | J-005007-07 |
| HRI-4 | ggUcaggaaUaaaUUagaU | Dharmacon | J-005007-08 |
| PKR-1 | gUaagggaacUUUgcgaUa | Dharmacon | J-003527-09 |
| PKR-2 | gcgagaaacUagacaaagU | Dharmacon | J-003527-10 |
| PKR-3 | cgaccUaacacaUcUgaaa | Dharmacon | J-003527-11 |
| PKR-4 | ccacaUgaUaggaggUUUa | Dharmacon | J-003527-12 |
| PERK-1 | ccaaUgggaUagUgacgaa | Dharmacon | J-004883-09 |
| PERK-2 | ggUaggaUcUgaUgaaUUU | Dharmacon | J-004883-10 |
| PERK-3 | gcaaUUagccUUaagUUgU | Dharmacon | J-004883-11 |
| PERK-4 | aaaUUUggcUgaaagaUga | Dharmacon | J-004883-12 |
| GCN2-1 | cagcagaaaUcaUgUacga | Dharmacon | J-005314-05 |
| GCN2-2 | gcaaUUcUgUggUgcaUaa | Dharmacon | J-005314-06 |
| GCN2-3 | gaccaUcccUagUgacUUa | Dharmacon | J-005314-07 |
| GCN2-4 | ggaaaUUgcUagUUUgUca | Dharmacon | J-005314-08 |
| GCN2-5 | cccUUgUcUcggaUaaaga | Dharmacon | A-005314-17 |
| GCN2-6 | cUggaaUaaUggaaUgUUg | Dharmacon | A-005314-18 |
| GCN2-7 | UcaUUgagUUUgaagaaUU | Dharmacon | A-005314-19 |
| GCN2-8 | UcUUUgUcUUcUaaUagUc | Dharmacon | A-005314-20 |
| ATF4-1 | CAGAUUGGAUGUUGGAGAA | Dharmacon | J-005125-10 |
| ATF4-2 | CGACUUGGAUGCCCUGUUG | Dharmacon | J-005125-11 |
| ATF4-3 | GAAGAACGAGGCUCUAAAA | Dharmacon | J-005125-12 |
| ATF4-4 | GAGUAGGAAGCCAGACUA | Dharmacon | J-005125-13 |
| SLC3A2-1 | ggaccUUacUcccaacUac | Dharmacon | J-003542-09 |
| SLC3A2-2 | gaaUgagcgUUUUcUggUa | Dharmacon | J-003542-10 |
| SLC3A2-3 | gUUccaggUUcgggacaUa | Dharmacon | J-003542-11 |
| SLC3A2-4 | gcgcagaagUggUggcaca | Dharmacon | J-003542-12 |

asiRNAs used throughout these studies are highlighted in red.

**Supplementary File 5C. Oligonucleotides used for library prep, PCR, and qRT-PCR analysis.**

|  |  |
| --- | --- |
| **Primer Name** | **Primer Sequence** |
| 4F2-FP1 | 5’-TCTGGACCTTACTCCCAACTA-3’ |
| 4F2-RP1 | 5’-ATCAAGAGCCTGTCTTCACTG-3’ |
| HsATF4-FP | 5’-TCAAACCTCATGGGTTCTCC-3’ |
| HsATF4-RP | 5’-GTGTCATCCAACGTGGTCAG-3’ |
| sgRNA\_F | 5’-GCTTTATATATCTTGTGGAAAGGACGAAACACC-3’ |
| sgRNA\_R | 5’-CAAGTTGATAACGGACTAGCCTT-3’ |
| IlluminaAd\_F | 5’-ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGCTTTATATATCTTGTGGA-3’ |
| IlluminaAd\_F | 5’- GACTGGAGTTCAGACGTGTGCTCTTCCGATCTGCCAAGTTGATAACGGACTAGCCTT-3’ |
| 5’-adaptor | 5’-rGrUrUrCrArGrArGrUrUrCrUrArCrArGrUrCrCrGrArCrGrArUrC-3’ |
| RT primer | 5’-AGACGTGTGCTCTTCCGATCT-3’ |
| Illumina Multiplex  Primer | 5’-AATGATACGGCGACCACCGAGATCTACACGTTCAGAGTTCTACAGTCCGA-3’ |
| Illumina Barcode Primer | 5’-CAAGCAGAAGACGGCATACGAGATGCCTAAGTGACTGGAGTTCAGACGTGTGCTCTTCCGATCT-3’ |
| tRNAHis-FW | 5’-GCCGTGATCGTATAGTGG-3’ |
| tRNAHis-REV | 5’-GAGAATTCCATGGTGCCGTGACTCGG-3’ |

**Supplementary File 5D. Composition and dietary intake of essential amino acids from the drinking water.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Amino Acids** | **Molecular Mass (g/mol)** | **Percentage (%)** | **Dietary intake (mg/g/day)** |
| L-Arginine hydrochloride | 211 | 22.6% | 0.340 |
| L-Cystine | 240 | 4.3% | 0.064 |
| L-Histidine hydrochloride | 210 | 7.5% | 0.113 |
| L-Isoleucine | 131 | 9.4% | 0.141 |
| L-Leucine | 131 | 9.4% | 0.141 |
| L-Lysine hydrochloride | 183 | 13.0% | 0.195 |
| L-Methionine | 149 | 2.7% | 0.041 |
| L-Phenylalanine | 165 | 5.9% | 0.089 |
| L-Threonine | 119 | 8.5% | 0.128 |
| L-Tryptophan | 204 | 1.8% | 0.027 |
| L-Tyrosine | 181 | 6.4% | 0.097 |
| L-Valine | 117 | 8.4% | 0.126 |