## SI Table 1. CellAge Functional Enrichment Analysis of 153 senescence promoters. The table displays the results of DAVID analysis of enriched clusters of related functional terms. Clusters are ordered by enrichment score.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DAVID Annotation Cluster 1 - Enrichment Score: 19.99** | | | | |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| UP\_KEYWORDS | Kinase | 51 | 5.70E-35 | 1.20E-32 |
| UP\_SEQ\_FEATURE | binding site:ATP | 40 | 6.30E-27 | 4.10E-24 |
| UP\_SEQ\_FEATURE | domain:Protein kinase | 35 | 1.10E-23 | 3.50E-21 |
| INTERPRO | Protein kinase, catalytic domain | 36 | 1.50E-23 | 5.50E-21 |
| INTERPRO | Protein kinase-like domain | 37 | 2.30E-23 | 4.20E-21 |
| UP\_KEYWORDS | Serine/threonine-protein kinase | 32 | 2.30E-23 | 2.40E-21 |
| GOTERM\_MF\_DIRECT | protein serine/threonine kinase activity | 31 | 1.20E-20 | 4.10E-18 |
| INTERPRO | Protein kinase, ATP binding site | 30 | 3.10E-20 | 3.80E-18 |
| UP\_KEYWORDS | Transferase | 53 | 5.80E-20 | 4.10E-18 |
| GOTERM\_MF\_DIRECT | protein kinase activity | 29 | 4.90E-19 | 8.20E-17 |
| UP\_SEQ\_FEATURE | nucleotide phosphate-binding region:ATP | 41 | 7.70E-19 | 1.70E-16 |
| UP\_KEYWORDS | ATP-binding | 46 | 4.00E-18 | 1.70E-16 |
| UP\_SEQ\_FEATURE | active site:Proton acceptor | 34 | 4.50E-18 | 7.20E-16 |
| INTERPRO | Serine/threonine-protein kinase, active site | 26 | 4.60E-18 | 4.20E-16 |
| SMART | S\_TKc | 30 | 5.40E-18 | 5.50E-16 |
| GOTERM\_MF\_DIRECT | ATP binding | 48 | 1.80E-15 | 2.00E-13 |
| UP\_KEYWORDS | Nucleotide-binding | 48 | 2.30E-15 | 5.90E-14 |
| GOTERM\_BP\_DIRECT | protein phosphorylation | 28 | 3.30E-15 | 2.60E-12 |
| **DAVID Annotation Cluster 2 - Enrichment Score: 7.58** | | | | |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| GOTERM\_BP\_DIRECT | positive regulation of transcription from RNA polymerase II promoter | 39 | 4.20E-15 | 2.20E-12 |
| GOTERM\_BP\_DIRECT | positive regulation of transcription, DNA-templated | 28 | 6.50E-14 | 2.60E-11 |
| GOTERM\_CC\_DIRECT | nucleoplasm | 59 | 1.20E-12 | 5.60E-11 |
| UP\_KEYWORDS | Transcription regulation | 47 | 1.30E-10 | 2.30E-09 |
| UP\_KEYWORDS | Transcription | 47 | 3.40E-10 | 5.10E-09 |
| UP\_KEYWORDS | Activator | 21 | 7.50E-08 | 9.90E-07 |
| GOTERM\_MF\_DIRECT | transcription factor activity, sequence-specific DNA binding | 27 | 2.20E-07 | 8.20E-06 |
| UP\_KEYWORDS | DNA-binding | 35 | 3.70E-06 | 4.10E-05 |
| GOTERM\_BP\_DIRECT | transcription from RNA polymerase II promoter | 17 | 1.20E-05 | 9.50E-04 |
| GOTERM\_MF\_DIRECT | DNA binding | 33 | 1.50E-05 | 3.40E-04 |
| GOTERM\_MF\_DIRECT | sequence-specific DNA binding | 16 | 4.70E-05 | 9.20E-04 |
| GOTERM\_BP\_DIRECT | transcription, DNA-templated | 33 | 3.70E-04 | 1.40E-02 |
| GOTERM\_MF\_DIRECT | transcriptional activator activity, RNA polymerase II core promoter proximal region sequence-specific binding | 9 | 1.10E-03 | 1.40E-02 |
| **DAVID Annotation Cluster 3 Enrichment Score: 6.14** | | | | |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| UP\_SEQ\_FEATURE | cross-link:Glycyl lysine isopeptide (Lys-Gly) (interchain with G-Cter in SUMO) | 12 | 3.00E-10 | 3.20E-08 |
| GOTERM\_MF\_DIRECT | transcription factor binding | 15 | 1.90E-07 | 7.90E-06 |
| GOTERM\_CC\_DIRECT | nuclear chromatin | 11 | 4.00E-06 | 1.20E-04 |
| GOTERM\_MF\_DIRECT | transcription regulatory region DNA binding | 11 | 1.70E-05 | 3.60E-04 |
| GOTERM\_MF\_DIRECT | sequence-specific DNA binding | 16 | 4.70E-05 | 9.20E-04 |
| **DAVID Annotation Cluster 4 - Enrichment Score: 5.47** | | | | |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| KEGG\_PATHWAY | Influenza A | 18 | 1.70E-10 | 4.10E-09 |
| KEGG\_PATHWAY | Fc epsilon RI signaling pathway | 12 | 1.70E-09 | 2.40E-08 |
| KEGG\_PATHWAY | Toll-like receptor signaling pathway | 14 | 1.70E-09 | 2.30E-08 |
| KEGG\_PATHWAY | T cell receptor signaling pathway | 13 | 1.40E-08 | 1.60E-07 |
| KEGG\_PATHWAY | Epstein-Barr virus infection | 16 | 4.10E-08 | 3.50E-07 |
| KEGG\_PATHWAY | Osteoclast differentiation | 13 | 2.10E-07 | 1.50E-06 |
| KEGG\_PATHWAY | TNF signaling pathway | 10 | 1.40E-05 | 7.40E-05 |
| KEGG\_PATHWAY | VEGF signaling pathway | 8 | 1.90E-05 | 9.30E-05 |
| KEGG\_PATHWAY | Toxoplasmosis | 10 | 3.40E-05 | 1.50E-04 |
| KEGG\_PATHWAY | Rap1 signaling pathway | 10 | 2.40E-03 | 7.00E-03 |
| KEGG\_PATHWAY | Tuberculosis | 9 | 3.10E-03 | 8.30E-03 |
| KEGG\_PATHWAY | Leishmaniasis | 5 | 1.70E-02 | 4.00E-02 |
| KEGG\_PATHWAY | Platelet activation | 5 | 1.10E-01 | 2.00E-01 |
| **DAVID Annotation Cluster 5 - Enrichment Score: 3.97** | | | | |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| KEGG\_PATHWAY | Glioma | 13 | 5.60E-11 | 1.60E-09 |
| KEGG\_PATHWAY | Melanoma | 13 | 1.70E-10 | 3.60E-09 |
| KEGG\_PATHWAY | Cell cycle | 13 | 1.10E-07 | 8.90E-07 |
| GOTERM\_MF\_DIRECT | kinase activity | 14 | 1.90E-07 | 9.00E-06 |
| KEGG\_PATHWAY | Pancreatic cancer | 10 | 2.20E-07 | 1.50E-06 |
| GOTERM\_MF\_DIRECT | cyclin-dependent protein serine/threonine kinase inhibitor activity | 5 | 1.70E-06 | 5.30E-05 |
| BIOCARTA | Cell Cycle | 9 | 3.90E-06 | 3.30E-04 |
| BIOCARTA | Influence of Ras and Rho proteins on G1 to S Transition | 8 | 2.10E-05 | 8.70E-04 |
| GOTERM\_BP\_DIRECT | negative regulation of phosphorylation | 5 | 2.50E-05 | 1.60E-03 |
| BIOCARTA | Cyclins and Cell Cycle Regulation | 7 | 1.40E-04 | 3.90E-03 |
| INTERPRO | Cyclin-dependent kinase inhibitor | 3 | 1.90E-04 | 8.90E-03 |
| GOTERM\_BP\_DIRECT | negative regulation of cyclin-dependent protein serine/threonine kinase activity | 4 | 9.10E-04 | 2.80E-02 |
| KEGG\_PATHWAY | Small cell lung cancer | 7 | 1.10E-03 | 3.30E-03 |
| BBID | 1.RBphosphoE2F | 6 | 1.20E-03 | 6.80E-02 |
| GOTERM\_BP\_DIRECT | G1/S transition of mitotic cell cycle | 6 | 2.10E-03 | 5.40E-02 |
| BIOCARTA | p53 Signaling Pathway | 5 | 2.20E-03 | 4.50E-02 |
| UP\_KEYWORDS | Cyclin | 4 | 3.10E-03 | 2.00E-02 |
| UP\_KEYWORDS | Protein kinase inhibitor | 3 | 4.50E-03 | 2.70E-02 |
| GOTERM\_BP\_DIRECT | regulation of cyclin-dependent protein serine/threonine kinase activity | 4 | 4.90E-03 | 9.40E-02 |
| BBID | 94.E2F\_transcriptional\_activity\_cell\_cycle | 4 | 7.80E-03 | 2.00E-01 |
| BBID | 26.cyclin-CDK\_complexes | 5 | 1.30E-02 | 1.70E-01 |
| BIOCARTA | Tumor Suppressor Arf Inhibits Ribosomal Biogenesis | 4 | 2.20E-02 | 1.70E-01 |
| UP\_SEQ\_FEATURE | short sequence motif:Nuclear localization signal | 7 | 4.60E-02 | 7.70E-01 |
| BIOCARTA | BTG family proteins and cell cycle regulation | 3 | 5.30E-02 | 2.50E-01 |
| BIOCARTA | Regulation of p27 Phosphorylation during Cell Cycle Progression | 3 | 7.10E-02 | 3.10E-01 |

## SI Table 2. CellAge Functional Enrichment Analysis of 121 senescence inhibitors. The table displays the results of DAVID analysis of enriched clusters of related functional terms. Clusters are ordered by enrichment score.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Annotation Cluster 1** | **Enrichment Score: 6.88** |  |  |  |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| GOTERM\_BP\_DIRECT | negative regulation of transcription from RNA polymerase II promoter | 28 | 3.00E-13 | 4.30E-10 |
| GOTERM\_BP\_DIRECT | negative regulation of transcription, DNA-templated | 19 | 8.00E-09 | 5.80E-06 |
| UP\_KEYWORDS | Repressor | 18 | 3.70E-08 | 1.10E-06 |
| UP\_KEYWORDS | Activator | 17 | 9.40E-07 | 1.60E-05 |
| UP\_KEYWORDS | Transcription regulation | 33 | 1.20E-06 | 1.90E-05 |
| UP\_KEYWORDS | Transcription | 33 | 2.20E-06 | 3.00E-05 |
| GOTERM\_BP\_DIRECT | transcription, DNA-templated | 25 | 3.10E-03 | 1.10E-01 |
| **Annotation Cluster 2** | **Enrichment Score: 5.06** |  |  |  |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| UP\_KEYWORDS | Cell cycle | 23 | 1.20E-11 | 6.10E-10 |
| UP\_SEQ\_FEATURE | active site:Proton acceptor | 20 | 8.80E-09 | 2.10E-06 |
| UP\_KEYWORDS | Serine/threonine-protein kinase | 15 | 4.70E-08 | 1.20E-06 |
| INTERPRO | Protein kinase-like domain | 17 | 2.00E-07 | 6.60E-05 |
| UP\_SEQ\_FEATURE | domain:Protein kinase | 15 | 6.20E-07 | 9.80E-05 |
| INTERPRO | Protein kinase, ATP binding site | 14 | 7.70E-07 | 1.30E-04 |
| UP\_KEYWORDS | Cell division | 13 | 2.00E-06 | 3.00E-05 |
| INTERPRO | Protein kinase, catalytic domain | 15 | 2.10E-06 | 2.30E-04 |
| UP\_KEYWORDS | Mitosis | 11 | 2.40E-06 | 3.10E-05 |
| UP\_KEYWORDS | Kinase | 17 | 3.70E-06 | 4.60E-05 |
| UP\_SEQ\_FEATURE | binding site:ATP | 15 | 3.80E-06 | 4.50E-04 |
| INTERPRO | Serine/threonine-protein kinase, active site | 12 | 4.20E-06 | 3.40E-04 |
| GOTERM\_MF\_DIRECT | protein serine/threonine kinase activity | 13 | 1.10E-05 | 1.20E-03 |
| UP\_SEQ\_FEATURE | nucleotide phosphate-binding region:ATP | 19 | 1.40E-05 | 1.30E-03 |
| SMART | S\_TKc | 13 | 1.80E-05 | 1.70E-03 |
| GOTERM\_BP\_DIRECT | peptidyl-serine phosphorylation | 8 | 2.40E-05 | 3.90E-03 |
| UP\_KEYWORDS | ATP-binding | 22 | 3.00E-05 | 3.10E-04 |
| UP\_KEYWORDS | Transferase | 24 | 7.10E-05 | 7.10E-04 |
| GOTERM\_BP\_DIRECT | cell division | 11 | 1.50E-04 | 1.10E-02 |
| GOTERM\_MF\_DIRECT | protein kinase activity | 11 | 1.80E-04 | 1.30E-02 |
| GOTERM\_BP\_DIRECT | protein phosphorylation | 12 | 3.00E-04 | 1.90E-02 |
| UP\_KEYWORDS | Cytoskeleton | 17 | 6.50E-04 | 5.20E-03 |
| UP\_KEYWORDS | Nucleotide-binding | 22 | 9.60E-04 | 7.10E-03 |
| GOTERM\_MF\_DIRECT | ATP binding | 22 | 1.20E-03 | 4.10E-02 |
| GOTERM\_BP\_DIRECT | mitotic nuclear division | 8 | 1.60E-03 | 6.30E-02 |
| GOTERM\_BP\_DIRECT | protein autophosphorylation | 6 | 6.60E-03 | 1.80E-01 |
| **Annotation Cluster 3** | **Enrichment Score: 3.59** |  |  |  |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| UP\_KEYWORDS | Mitosis | 11 | 2.40E-06 | 3.10E-05 |
| UP\_KEYWORDS | Chromosome | 11 | 9.00E-05 | 8.50E-04 |
| UP\_KEYWORDS | Centromere | 6 | 1.10E-03 | 7.50E-03 |
| UP\_KEYWORDS | Kinetochore | 4 | 1.80E-02 | 9.10E-02 |

## SI Table 3. genes with one2one homology with human genes and confidence score of 1.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Species** | **Homologues** | **CellAge homologues** | **% Homologues** | **% CellAge homologues** |
| Yeast | 654 | 3 | 2.93 | 1.08 |
| Worm | 1430 | 17 | 6.40 | 6.09 |
| Fly | 2314 | 28 | 10.35 | 10.04 |
| Mouse | 15215 | 242 | 68.05 | 86.74 |
| Rat | 14150 | 228 | 63.29 | 81.72 |
| Monkey | 15129 | 235 | 67.67 | 84.23 |

## SI Table 4. Statistical effect of research focus on CellAge/GenAge overlap. Subsetting the data for publication bias and calculating the GenAge and CellAge intersect. P-values are calculated using Fisher’s exact test.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Publication Filter** | **CellAge Genes** | **Overlap** | **GenAge genes** | **Total genes** | **P-value** |
| <= 100 | 139 | 5 | 86 | 16880 | **7.66E-05** |
| <= 500 | 217 | 15 | 196 | 18530 | **1.36E-09** |
| <= 1000 | 235 | 22 | 228 | 18852 | **1.19E-14** |
| <= 2000 | 254 | 30 | 260 | 19059 | **1.12E-20** |
| <= 3000 | 263 | 33 | 269 | 19148 | **5.32E-23** |
| >= 100 | 137 | 38 | 219 | 2456 | **5.98E-12** |
| >= 500 | 58 | 27 | 106 | 776 | **2.29E-11** |
| >= 1000 | 40 | 20 | 74 | 456 | **2.15E-08** |
| >= 2000 | 21 | 12 | 42 | 248 | **1.24E-06** |
| >= 3000 | 12 | 9 | 33 | 158 | **2.25E-06** |

## SI Table 5. Functional Enrichment GO terms between CellAge Senescence Promoter Genes and Genes Upregulated with Age.

|  |  |  |
| --- | --- | --- |
| **geneset** | **PValue** | **FDR** |
| GO:2000112 | 4.64E-07 | 0.000736 |
| GO:0006357 | 5.26E-07 | 0.000736 |
| GO:0010556 | 9.71E-07 | 0.000905 |
| GO:0006366 | 1.76E-06 | 0.00096 |
| GO:0031326 | 2.40E-06 | 0.00096 |
| GO:0051171 | 3.13E-06 | 0.00096 |
| GO:0009889 | 3.35E-06 | 0.00096 |
| GO:0034645 | 3.35E-06 | 0.00096 |
| GO:0010629 | 4.12E-06 | 0.00096 |
| GO:0006355 | 4.21E-06 | 0.00096 |
| GO:0048731 | 4.46E-06 | 0.00096 |
| GO:1903506 | 4.54E-06 | 0.00096 |
| GO:2001141 | 4.88E-06 | 0.00096 |
| GO:0019219 | 5.66E-06 | 0.00096 |
| GO:0010468 | 5.97E-06 | 0.00096 |
| GO:0006351 | 6.07E-06 | 0.00096 |
| GO:0044271 | 6.35E-06 | 0.00096 |
| GO:0048513 | 6.35E-06 | 0.00096 |
| GO:0097659 | 6.52E-06 | 0.00096 |
| GO:0009059 | 7.65E-06 | 0.00105 |
| GO:0034654 | 7.88E-06 | 0.00105 |
| GO:0019438 | 8.98E-06 | 0.001127 |
| GO:0051252 | 9.26E-06 | 0.001127 |
| GO:0032774 | 9.93E-06 | 0.001143 |
| GO:0018130 | 1.02E-05 | 0.001143 |
| GO:1901362 | 1.69E-05 | 0.001816 |
| GO:0044707 | 1.81E-05 | 0.001878 |
| GO:0007275 | 2.04E-05 | 0.002041 |
| GO:0090304 | 3.26E-05 | 0.003142 |
| GO:0010467 | 3.46E-05 | 0.003227 |
| GO:0032501 | 4.61E-05 | 0.00416 |
| GO:0016070 | 4.91E-05 | 0.004227 |
| GO:0051254 | 4.99E-05 | 0.004227 |
| GO:0009605 | 5.68E-05 | 0.004672 |
| GO:2000113 | 6.00E-05 | 0.004796 |
| GO:0045892 | 6.25E-05 | 0.004858 |
| GO:0000122 | 7.80E-05 | 0.005887 |
| GO:0048511 | 8.00E-05 | 0.005887 |
| GO:1903507 | 8.77E-05 | 0.006286 |
| GO:1902679 | 9.77E-05 | 0.006834 |
| GO:0051172 | 0.000107 | 0.007245 |
| GO:0051253 | 0.000109 | 0.007245 |
| GO:0048856 | 0.000122 | 0.007805 |
| GO:0048608 | 0.000126 | 0.007805 |
| GO:0061458 | 0.000126 | 0.007805 |
| GO:0048522 | 0.00014 | 0.008206 |
| GO:0010558 | 0.000141 | 0.008206 |
| GO:0031327 | 0.000141 | 0.008206 |
| GO:0010557 | 0.000162 | 0.008605 |
| GO:0048518 | 0.000163 | 0.008605 |
| GO:0045893 | 0.000168 | 0.008605 |
| GO:1903508 | 0.000168 | 0.008605 |
| GO:0006139 | 0.000173 | 0.008605 |
| GO:0031324 | 0.000178 | 0.008605 |
| GO:1902680 | 0.000183 | 0.008605 |
| GO:0032607 | 0.00019 | 0.008605 |
| GO:0032647 | 0.00019 | 0.008605 |
| GO:0032727 | 0.00019 | 0.008605 |
| GO:0044249 | 0.000194 | 0.008605 |
| GO:0048869 | 0.000194 | 0.008605 |
| GO:0009890 | 0.0002 | 0.008605 |
| GO:0045934 | 0.0002 | 0.008605 |
| GO:0045944 | 0.0002 | 0.008605 |
| GO:0010033 | 0.000201 | 0.008605 |
| GO:0046483 | 0.000201 | 0.008605 |
| GO:0045935 | 0.000205 | 0.008605 |
| GO:0010604 | 0.000206 | 0.008605 |
| GO:0042089 | 0.000219 | 0.009024 |
| GO:0010605 | 0.000229 | 0.009274 |
| GO:0006725 | 0.000232 | 0.009278 |
| GO:1901576 | 0.000245 | 0.009666 |
| GO:0034641 | 0.000269 | 0.010396 |
| GO:0042107 | 0.000275 | 0.010396 |
| GO:0045444 | 0.000275 | 0.010396 |
| GO:0045595 | 0.00028 | 0.010458 |
| GO:0006807 | 0.000291 | 0.010726 |
| GO:0009892 | 0.00033 | 0.011974 |
| GO:1901360 | 0.00034 | 0.012184 |
| GO:0009058 | 0.000353 | 0.012487 |
| GO:0031325 | 0.000369 | 0.012876 |
| GO:0030154 | 0.000373 | 0.012876 |
| GO:0009719 | 0.000387 | 0.013208 |
| GO:0045667 | 0.000403 | 0.013588 |
| GO:0044767 | 0.00041 | 0.013651 |
| GO:0003006 | 0.000416 | 0.013673 |
| GO:0031328 | 0.00045 | 0.014626 |
| GO:0007167 | 0.000479 | 0.015291 |
| GO:0051173 | 0.000481 | 0.015291 |
| GO:0048523 | 0.000523 | 0.016435 |
| GO:0007623 | 0.000539 | 0.01658 |
| GO:0032481 | 0.000539 | 0.01658 |
| GO:0009893 | 0.00058 | 0.017624 |
| GO:0071216 | 0.000605 | 0.018183 |
| GO:0032502 | 0.000615 | 0.018289 |
| GO:0009891 | 0.000626 | 0.018433 |
| GO:0032648 | 0.00064 | 0.018452 |
| GO:0032728 | 0.00064 | 0.018452 |
| GO:0042221 | 0.000797 | 0.022733 |
| GO:0009607 | 0.00086 | 0.024067 |
| GO:0060429 | 0.00086 | 0.024067 |
| GO:0032479 | 0.000905 | 0.024826 |
| GO:0032606 | 0.000905 | 0.024826 |
| GO:0032608 | 0.001005 | 0.027289 |
| GO:0007050 | 0.001019 | 0.027418 |
| GO:0060255 | 0.001059 | 0.028102 |
| GO:0000003 | 0.001075 | 0.028102 |
| GO:0022414 | 0.001075 | 0.028102 |
| GO:0007166 | 0.001118 | 0.028376 |
| GO:0071310 | 0.001126 | 0.028376 |
| GO:0042035 | 0.001142 | 0.028376 |
| GO:0009991 | 0.001146 | 0.028376 |
| GO:0031323 | 0.001146 | 0.028376 |
| GO:0080090 | 0.001146 | 0.028376 |
| GO:0014070 | 0.001158 | 0.028422 |
| GO:0050673 | 0.00129 | 0.031364 |
| GO:0042127 | 0.00131 | 0.031576 |
| GO:0010628 | 0.00134 | 0.032044 |
| GO:0048519 | 0.001395 | 0.033076 |
| GO:0044260 | 0.00143 | 0.033613 |
| GO:1903706 | 0.001446 | 0.033708 |
| GO:0033993 | 0.001646 | 0.038044 |
| GO:0001817 | 0.001739 | 0.039259 |
| GO:0007548 | 0.00174 | 0.039259 |
| GO:0031668 | 0.00174 | 0.039259 |
| GO:0045786 | 0.002005 | 0.044874 |
| GO:0051239 | 0.00204 | 0.045072 |
| GO:0000086 | 0.002074 | 0.045072 |
| GO:0090100 | 0.002074 | 0.045072 |
| GO:0000075 | 0.002109 | 0.045072 |
| GO:0031100 | 0.002109 | 0.045072 |
| GO:0071496 | 0.002111 | 0.045072 |

## SI Table 6. Actual and Expected Number of CellAge Genes Expressed in a Tissue-Specific Manner.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Tissue** | **p-Value** | **Corrected p-Value** | **Actual tissue-specific gene expression** | **Expected tissue-specific gene expression** |
| Adipose Tissue | 1 | 1 | 0 | 0.37566 |
| Adrenal Gland | 1 | 1 | 0 | 0.85246 |
| Bladder | 1 | 1 | 0 | 0.910254 |
| Blood | 0.785293 | 1 | 4 | 3.59767 |
| Blood Vessel | 0.334885 | 1 | 1 | 0.404557 |
| Brain | 0.199985 | 1 | 4 | 7.787727 |
| Breast | 1 | 1 | 0 | 0.447903 |
| Cervix Uteri | 1 | 1 | 0 | 0.202279 |
| Colon | 1 | 1 | 0 | 0.549042 |
| Esophagus | 1 | 1 | 0 | 0.505697 |
| Fallopian Tube | 0.424416 | 1 | 0 | 1.733817 |
| Heart | 1 | 1 | 0 | 0.751321 |
| Kidney | 1 | 1 | 1 | 1.51709 |
| Liver | 0.191911 | 1 | 1 | 3.7855 |
| Lung | 1 | 1 | 1 | 1.025842 |
| Muscle | 1 | 1 | 2 | 2.253962 |
| Nerve | 0.408287 | 1 | 0 | 1.401502 |
| Ovary | 1 | 1 | 1 | 1.069187 |
| Pancreas | 0.630233 | 1 | 0 | 1.083635 |
| Pituitary | 0.774019 | 1 | 2 | 3.149767 |
| Prostate | 0.576829 | 1 | 1 | 0.85246 |
| Salivary Gland | 0.617944 | 1 | 1 | 0.953599 |
| Skin | 0.135968 | 1 | 1 | 4.146712 |
| Small Intestine | 0.737681 | 1 | 1 | 2.427343 |
| Spleen | 0.732728 | 1 | 1 | 2.311756 |
| Stomach | 0.576829 | 1 | 1 | 0.85246 |
| Testis | 1.45E-06 | 4.34E-05 | 4 | 22.98752 |
| Thyroid | 0.636728 | 1 | 0 | 1.213672 |
| Uterus | 1 | 1 | 0 | 0.361212 |
| Vagina | 0.629461 | 1 | 0 | 1.054738 |

## SI Table 7. Percent Difference between Actual and Expected Number of CellAge Genes Differentially Expressed with Age across Different Tissues.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Tissue** | **P-value** | **Corrected p-Value** | **Actual** | **Expected** | **% Difference** | **Expression** |
| Adipose | 1 | 1 | 2 | 2.16084 | -7.73114 | Under |
| Adrenal Gland | 0.406471 | 1 | 2 | 1.391226 | 35.90289 | Under |
| Blood | 1 | 1 | 0 | 0.059201 | NA | Under |
| Blood Vessel | 0.752932 | 1 | 3 | 2.69365 | 10.7611 | Under |
| Brain | 0.591462 | 1 | 6 | 8.302955 | -32.2025 | Under |
| Breast | 1 | 1 | 0 | 0.148003 | NA | Under |
| Colon | 0.001298 | 0.033754427 | 24 | 11.79582 | 68.18774 | Under |
| Esophagus | 1 | 1 | 0 | 0.207204 | NA | Under |
| Heart | 0.441285 | 1 | 1 | 0.577211 | 53.61227 | Under |
| Liver | 1 | 1 | 0 | 0.088802 | NA | Under |
| Lung | 0.020094 | 0.522444911 | 8 | 3.359663 | 81.69851 | Under |
| Muscle | 1 | 1 | 1 | 1.021219 | -2.09963 | Under |
| Nerve | 0.635089 | 1 | 3 | 4.632486 | -42.7773 | Under |
| Ovary | 0.123517 | 1 | 9 | 5.446502 | 49.19528 | Under |
| Pancreas | 1 | 1 | 0 | 0.177603 | NA | Under |
| Pituitary | 1 | 1 | 0 | 0.0148 | NA | Under |
| Prostate | 0.707184 | 1 | 8 | 7.355737 | 8.391169 | Under |
| Salivary Gland | 1 | 1 | 1 | 1.894435 | -61.8038 | Under |
| Skin | 1 | 1 | 0 | 0.222004 | NA | Under |
| Spleen | 1 | 1 | 0 | 0.0148 | NA | Under |
| Stomach | 1 | 1 | 0 | 0.236804 | NA | Under |
| Testis | 1 | 1 | 0 | 0.088802 | NA | Under |
| Thyroid | 1 | 1 | 0 | 0.310806 | NA | Under |
| Uterus | 0.620125 | 1 | 11 | 9.694181 | 12.62016 | Under |
| Vagina | 1 | 1 | 0 | 0.118402 | NA | Under |
| Adipose | 1 | 1 | 3 | 3.182059 | -5.88992 | Over |
| Adrenal Gland | 0.051812 | 1 | 5 | 2.012838 | 85.19126 | Over |
| Blood | 0.000822 | 0.021366139 | 3 | 0.192404 | 175.8923 | Over |
| Blood Vessel | 0.099006 | 1 | 24 | 16.99072 | 34.19937 | Over |
| Brain | 0.000142 | 0.003696598 | 27 | 12.12143 | 76.06356 | Over |
| Breast | 0.163751 | 1 | 2 | 0.725214 | 93.55498 | Over |
| Colon | 0.22914 | 1 | 7 | 4.558485 | 42.24628 | Over |
| Esophagus | 0.65804 | 1 | 2 | 1.450427 | 31.85536 | Over |
| Heart | 0.236447 | 1 | 5 | 3.048857 | 48.48249 | Over |
| Liver | 1 | 1 | 0 | 0.148003 | NA | Over |
| Lung | 0.171585 | 1 | 8 | 5.046894 | 45.2691 | Over |
| Muscle | 0.245387 | 1 | 7 | 4.736088 | 38.58035 | Over |
| Nerve | 1 | 1 | 3 | 3.936873 | -27.0114 | Over |
| Ovary | 1 | 1 | 3 | 3.315262 | -9.98412 | Over |
| Pancreas | 1 | 1 | 0 | 0.236804 | NA | Over |
| Pituitary | 1 | 1 | 0 | 0.0148 | NA | Over |
| Prostate | 0.058393 | 1 | 15 | 9.087369 | 49.0932 | Over |
| Salivary Gland | 0.116898 | 1 | 11 | 6.896929 | 45.85224 | Over |
| Skin | 1 | 1 | 1 | 1.139621 | -13.051 | Over |
| Small Intestine | 1 | 1 | 0 | 0.0148 | NA | Over |
| Spleen | 1 | 1 | 0 | 0.044401 | NA | Over |
| Stomach | 0.009081 | 0.236116927 | 2 | 0.148003 | 172.439 | Over |
| Testis | 0.013681 | 0.355704667 | 3 | 0.503209 | 142.543 | Over |
| Thyroid | 0.072402 | 1 | 2 | 0.444008 | 127.3311 | Over |
| Uterus | 0.055427 | 1 | 13 | 7.370537 | 55.27063 | Over |
| Vagina | 1 | 1 | 0 | 0.162803 | NA | Over |

## SI Table 8. Up and Downregulation of CellAge Senescence Promoters and Inhibitors in Different Tissue with Age.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Tissue | P-value | Corrected P-Value | Actual | Expected | Difference | log(p-value) | Effect | Regulation |
| Adipose | 0.329626 | 1 | 2 | 1.177232 | 0.822768 | 1.10979639 | Promotes | Down |
| Adrenal Gland | 0.533691 | 1 | 1 | 0.757944 | 0.242056 | 0.62793784 | Promotes | Down |
| Blood | 1 | 1 | 0 | 0.032253 | -0.03225 | 0 | Promotes | Down |
| Blood Vessel | 0.660138 | 1 | 2 | 1.467508 | 0.532492 | 0.41530583 | Promotes | Down |
| Brain | 0.333896 | 1 | 2 | 4.523474 | -2.52347 | 1.09692702 | Promotes | Down |
| Breast | 1 | 1 | 0 | 0.080632 | -0.08063 | 0 | Promotes | Down |
| Colon | 0.038576 | 1 | 12 | 6.426396 | 5.573604 | 3.2551206 | Promotes | Down |
| Esophagus | 1 | 1 | 0 | 0.112885 | -0.11289 | 0 | Promotes | Down |
| Heart | 0.270985 | 1 | 1 | 0.314466 | 0.685534 | 1.30569253 | Promotes | Down |
| Liver | 1 | 1 | 0 | 0.048379 | -0.04838 | 0 | Promotes | Down |
| Lung | 0.705995 | 1 | 2 | 1.830354 | 0.169646 | 0.34814702 | Promotes | Down |
| Muscle | 0.428581 | 1 | 1 | 0.556363 | 0.443637 | 0.84727582 | Promotes | Down |
| Nerve | 0.524855 | 1 | 1 | 2.523792 | -1.52379 | 0.64463377 | Promotes | Down |
| Ovary | 0.772409 | 1 | 3 | 2.96727 | 0.03273 | 0.25824104 | Promotes | Down |
| Pancreas | 1 | 1 | 0 | 0.096759 | -0.09676 | 0 | Promotes | Down |
| Pituitary | 1 | 1 | 0 | 0.008063 | -0.00806 | 1.11E-16 | Promotes | Down |
| Prostate | 0.604539 | 1 | 5 | 4.007427 | 0.992573 | 0.50328852 | Promotes | Down |
| Salivary Gland | 1 | 1 | 1 | 1.032094 | -0.03209 | 1.11E-16 | Promotes | Down |
| Skin | 1 | 1 | 0 | 0.120948 | -0.12095 | 2.22E-16 | Promotes | Down |
| Small Intestine | NA | NA | NA | NA | NA | NA | Promotes | Down |
| Spleen | 1 | 1 | 0 | 0.008063 | -0.00806 | 1.11E-16 | Promotes | Down |
| Stomach | 1 | 1 | 0 | 0.129012 | -0.12901 | 0 | Promotes | Down |
| Testis | 1 | 1 | 0 | 0.048379 | -0.04838 | 0 | Promotes | Down |
| Thyroid | 1 | 1 | 0 | 0.169328 | -0.16933 | 0 | Promotes | Down |
| Uterus | 0.069164 | 1 | 1 | 5.281417 | -4.28142 | 2.67127667 | Promotes | Down |
| Vagina | 1 | 1 | 0 | 0.064506 | -0.06451 | 0 | Promotes | Down |
| Adipose | 0.250958 | 1 | 3 | 1.733595 | 1.266405 | 1.38246941 | Promotes | Up |
| Adrenal Gland | 0.00493 | 0.128184 | 5 | 1.0966 | 3.9034 | 5.31238486 | Promotes | Up |
| Blood | 0.004753 | 0.123569 | 2 | 0.104822 | 1.895178 | 5.34904948 | Promotes | Up |
| Blood Vessel | 0.038043 | 0.989127 | 16 | 9.256591 | 6.743409 | 3.26902862 | Promotes | Up |
| Brain | 2.69E-06 | 6.99E-05 | 21 | 6.603788 | 14.39621 | 12.8259869 | Promotes | Up |
| Breast | 0.059375 | 1 | 2 | 0.395098 | 1.604902 | 2.82388333 | Promotes | Up |
| Colon | 0.03891 | 1 | 6 | 2.483476 | 3.516524 | 3.24649769 | Promotes | Up |
| Esophagus | 0.187175 | 1 | 2 | 0.790197 | 1.209803 | 1.67570953 | Promotes | Up |
| Heart | 0.02587 | 0.672632 | 5 | 1.661026 | 3.338974 | 3.65465416 | Promotes | Up |
| Liver | 1 | 1 | 0 | 0.080632 | -0.08063 | 0 | Promotes | Up |
| Lung | 0.203689 | 1 | 5 | 2.749562 | 2.250438 | 1.59116301 | Promotes | Up |
| Muscle | 0.331845 | 1 | 4 | 2.580234 | 1.419766 | 1.1030866 | Promotes | Up |
| Nerve | 0.477181 | 1 | 3 | 2.14482 | 0.85518 | 0.73986013 | Promotes | Up |
| Ovary | 1 | 1 | 1 | 1.806164 | -0.80616 | 0 | Promotes | Up |
| Pancreas | 1 | 1 | 0 | 0.129012 | -0.12901 | 0 | Promotes | Up |
| Pituitary | 1 | 1 | 0 | 0.008063 | -0.00806 | 1.11E-16 | Promotes | Up |
| Prostate | 0.017488 | 0.454682 | 11 | 4.950825 | 6.049175 | 4.04625287 | Promotes | Up |
| Salivary Gland | 0.057312 | 1 | 8 | 3.757466 | 4.242534 | 2.85924986 | Promotes | Up |
| Skin | 0.464552 | 1 | 1 | 0.620869 | 0.379131 | 0.76668267 | Promotes | Up |
| Small Intestine | 1 | 1 | 0 | 0.008063 | -0.00806 | 1.11E-16 | Promotes | Up |
| Spleen | 1 | 1 | 0 | 0.02419 | -0.02419 | 0 | Promotes | Up |
| Stomach | 0.002786 | 0.07243 | 2 | 0.080632 | 1.919368 | 5.88322826 | Promotes | Up |
| Testis | 0.030615 | 0.796002 | 2 | 0.27415 | 1.72585 | 3.48624998 | Promotes | Up |
| Thyroid | 0.21578 | 1 | 1 | 0.241897 | 0.758103 | 1.53349744 | Promotes | Up |
| Uterus | 0.065756 | 1 | 8 | 4.01549 | 3.98451 | 2.72180487 | Promotes | Up |
| Vagina | 1 | 1 | 0 | 0.088696 | -0.0887 | 0 | Promotes | Up |
| Adipose | 1 | 1 | 0 | 0.944884 | -0.94488 | 0 | Inhibits | Down |
| Adrenal Gland | 0.457649 | 1 | 1 | 0.60835 | 0.39165 | 0.78165238 | Inhibits | Down |
| Blood | 1 | 1 | 0 | 0.025887 | -0.02589 | 0 | Inhibits | Down |
| Blood Vessel | 1 | 1 | 1 | 1.177869 | -0.17787 | 0 | Inhibits | Down |
| Brain | 1 | 1 | 3 | 3.630683 | -0.63068 | 1.11E-16 | Inhibits | Down |
| Breast | 1 | 1 | 0 | 0.064718 | -0.06472 | 0 | Inhibits | Down |
| Colon | 0.00554 | 0.144045 | 12 | 5.158029 | 6.841971 | 5.19572356 | Inhibits | Down |
| Esophagus | 1 | 1 | 0 | 0.090605 | -0.09061 | 0 | Inhibits | Down |
| Heart | 1 | 1 | 0 | 0.2524 | -0.2524 | 0 | Inhibits | Down |
| Liver | 1 | 1 | 0 | 0.038831 | -0.03883 | 0 | Inhibits | Down |
| Lung | 0.016122 | 0.41918 | 5 | 1.4691 | 3.5309 | 4.12755221 | Inhibits | Down |
| Muscle | 1 | 1 | 0 | 0.446555 | -0.44655 | 1.11E-16 | Inhibits | Down |
| Nerve | 1 | 1 | 2 | 2.025675 | -0.02568 | 0 | Inhibits | Down |
| Ovary | 0.032573 | 0.84689 | 6 | 2.381624 | 3.618376 | 3.42428098 | Inhibits | Down |
| Pancreas | 1 | 1 | 0 | 0.077662 | -0.07766 | 0 | Inhibits | Down |
| Pituitary | 1 | 1 | 0 | 0.006472 | -0.00647 | 0 | Inhibits | Down |
| Prostate | 0.774212 | 1 | 2 | 3.216487 | -1.21649 | 0.25590938 | Inhibits | Down |
| Salivary Gland | 1 | 1 | 0 | 0.828391 | -0.82839 | 0 | Inhibits | Down |
| Skin | 1 | 1 | 0 | 0.097077 | -0.09708 | 1.11E-16 | Inhibits | Down |
| Small Intestine | NA | NA | NA | NA | NA | NA | Inhibits | Down |
| Spleen | 1 | 1 | 0 | 0.006472 | -0.00647 | 0 | Inhibits | Down |
| Stomach | 1 | 1 | 0 | 0.103549 | -0.10355 | 1.11E-16 | Inhibits | Down |
| Testis | 1 | 1 | 0 | 0.038831 | -0.03883 | 0 | Inhibits | Down |
| Thyroid | 1 | 1 | 0 | 0.135908 | -0.13591 | 0 | Inhibits | Down |
| Uterus | 0.010122 | 0.263163 | 10 | 4.239032 | 5.760968 | 4.59307837 | Inhibits | Down |
| Vagina | 1 | 1 | 0 | 0.051774 | -0.05177 | 1.11E-16 | Inhibits | Down |
| Adipose | 0.652033 | 1 | 0 | 1.391438 | -1.39144 | 0.4276599 | Inhibits | Up |
| Adrenal Gland | 1 | 1 | 0 | 0.880166 | -0.88017 | 2.22E-16 | Inhibits | Up |
| Blood | 0.080968 | 1 | 1 | 0.084133 | 0.915867 | 2.51370667 | Inhibits | Up |
| Blood Vessel | 0.848137 | 1 | 8 | 7.429632 | 0.570368 | 0.164713 | Inhibits | Up |
| Brain | 0.656031 | 1 | 6 | 5.300408 | 0.699592 | 0.42154722 | Inhibits | Up |
| Breast | 1 | 1 | 0 | 0.317118 | -0.31712 | 1.11E-16 | Inhibits | Up |
| Colon | 0.7262 | 1 | 1 | 1.993316 | -0.99332 | 0.31993048 | Inhibits | Up |
| Esophagus | 1 | 1 | 0 | 0.634237 | -0.63424 | 0 | Inhibits | Up |
| Heart | 0.646475 | 1 | 0 | 1.333192 | -1.33319 | 0.43622143 | Inhibits | Up |
| Liver | 1 | 1 | 0 | 0.064718 | -0.06472 | 0 | Inhibits | Up |
| Lung | 0.486862 | 1 | 3 | 2.206886 | 0.793114 | 0.71977437 | Inhibits | Up |
| Muscle | 0.465736 | 1 | 3 | 2.070978 | 0.929022 | 0.76413704 | Inhibits | Up |
| Nerve | 0.423304 | 1 | 0 | 1.7215 | -1.7215 | 0.85966359 | Inhibits | Up |
| Ovary | 0.658114 | 1 | 2 | 1.449684 | 0.550316 | 0.41837685 | Inhibits | Up |
| Pancreas | 1 | 1 | 0 | 0.103549 | -0.10355 | 1.11E-16 | Inhibits | Up |
| Pituitary | 1 | 1 | 0 | 0.006472 | -0.00647 | 0 | Inhibits | Up |
| Prostate | 1 | 1 | 4 | 3.973688 | 0.026312 | 0 | Inhibits | Up |
| Salivary Gland | 1 | 1 | 3 | 3.015861 | -0.01586 | 0 | Inhibits | Up |
| Skin | 1 | 1 | 0 | 0.498329 | -0.49833 | 0 | Inhibits | Up |
| Small Intestine | 1 | 1 | 0 | 0.006472 | -0.00647 | 0 | Inhibits | Up |
| Spleen | 1 | 1 | 0 | 0.019415 | -0.01942 | 0 | Inhibits | Up |
| Stomach | 1 | 1 | 0 | 0.064718 | -0.06472 | 0 | Inhibits | Up |
| Testis | 0.198244 | 1 | 1 | 0.220041 | 0.779959 | 1.6182582 | Inhibits | Up |
| Thyroid | 0.177112 | 1 | 1 | 0.194154 | 0.805846 | 1.73097093 | Inhibits | Up |
| Uterus | 0.258871 | 1 | 5 | 3.222959 | 1.777041 | 1.35142542 | Inhibits | Up |
| Vagina | 1 | 1 | 0 | 0.07119 | -0.07119 | 0 | Inhibits | Up |

## SI Table 9. Functional Enrichment GO terms between CellAge Senescence Promoter Genes and TSGs.

|  |  |  |
| --- | --- | --- |
| geneset | PValue | FDR |
| GO:2000134 | 7.11E-08 | 0.000182 |
| GO:1902807 | 1.03E-07 | 0.000182 |
| GO:0044772 | 3.09E-07 | 0.000227 |
| GO:0000082 | 3.54E-07 | 0.000227 |
| GO:0090398 | 5.53E-07 | 0.000227 |
| GO:0044770 | 5.55E-07 | 0.000227 |
| GO:0072331 | 5.55E-07 | 0.000227 |
| GO:0044843 | 5.68E-07 | 0.000227 |
| GO:0008283 | 5.80E-07 | 0.000227 |
| GO:2000045 | 7.15E-07 | 0.000252 |
| GO:0007093 | 9.51E-07 | 0.000295 |
| GO:0000075 | 1.11E-06 | 0.000295 |
| GO:0042127 | 1.18E-06 | 0.000295 |
| GO:0007569 | 1.25E-06 | 0.000295 |
| GO:1902806 | 1.25E-06 | 0.000295 |
| GO:1901991 | 1.64E-06 | 0.000361 |
| GO:1901988 | 2.12E-06 | 0.00044 |
| GO:0010948 | 2.79E-06 | 0.000547 |
| GO:0031571 | 3.38E-06 | 0.000567 |
| GO:0044783 | 3.38E-06 | 0.000567 |
| GO:0044819 | 3.38E-06 | 0.000567 |
| GO:0030330 | 3.85E-06 | 0.000617 |
| GO:1901990 | 5.24E-06 | 0.000804 |
| GO:0042770 | 6.52E-06 | 0.000958 |
| GO:1903047 | 7.26E-06 | 0.001025 |
| GO:1901987 | 7.78E-06 | 0.001056 |
| GO:0006974 | 1.89E-05 | 0.002473 |
| GO:0007568 | 2.06E-05 | 0.002601 |
| GO:0045930 | 2.30E-05 | 0.002798 |
| GO:0030856 | 3.48E-05 | 0.003839 |
| GO:0044773 | 3.48E-05 | 0.003839 |
| GO:0044774 | 3.48E-05 | 0.003839 |
| GO:0051348 | 3.76E-05 | 0.004021 |
| GO:0090399 | 4.65E-05 | 0.004823 |
| GO:0045786 | 5.35E-05 | 0.005392 |
| GO:0006338 | 5.67E-05 | 0.005553 |
| GO:1901796 | 7.83E-05 | 0.007468 |
| GO:0043086 | 0.00011 | 0.009954 |
| GO:0006977 | 0.000116 | 0.009954 |
| GO:0072431 | 0.000116 | 0.009954 |
| GO:1902400 | 0.000116 | 0.009954 |
| GO:0043588 | 0.000122 | 0.010244 |
| GO:0044092 | 0.000131 | 0.010524 |
| GO:0031324 | 0.000131 | 0.010524 |
| GO:0000077 | 0.000142 | 0.010858 |
| GO:0031570 | 0.000142 | 0.010858 |
| GO:0045616 | 0.000155 | 0.01093 |
| GO:0072401 | 0.000163 | 0.01093 |
| GO:0072413 | 0.000163 | 0.01093 |
| GO:0072422 | 0.000163 | 0.01093 |
| GO:1902402 | 0.000163 | 0.01093 |
| GO:1902403 | 0.000163 | 0.01093 |
| GO:0048869 | 0.000169 | 0.01093 |
| GO:0006469 | 0.000169 | 0.01093 |
| GO:0030855 | 0.00017 | 0.01093 |
| GO:0010564 | 0.000181 | 0.011396 |
| GO:0000278 | 0.000199 | 0.012295 |
| GO:0033554 | 0.00021 | 0.012692 |
| GO:0045604 | 0.000212 | 0.012692 |
| GO:0010605 | 0.000221 | 0.012955 |
| GO:0072395 | 0.000224 | 0.012955 |
| GO:0008285 | 0.000237 | 0.013502 |
| GO:0007346 | 0.000256 | 0.013935 |
| GO:0050673 | 0.000256 | 0.013935 |
| GO:0033673 | 0.000257 | 0.013935 |
| GO:0030216 | 0.000302 | 0.016144 |
| GO:0007049 | 0.000312 | 0.016413 |
| GO:0045682 | 0.000318 | 0.016503 |
| GO:0031400 | 0.000341 | 0.01743 |
| GO:0001816 | 0.000425 | 0.021186 |
| GO:0009892 | 0.000426 | 0.021186 |
| GO:0006325 | 0.000434 | 0.021273 |
| GO:0034644 | 0.00046 | 0.022215 |
| GO:0071901 | 0.000493 | 0.023486 |
| GO:0048519 | 0.000501 | 0.023486 |
| GO:0048523 | 0.000507 | 0.023486 |
| GO:0043487 | 0.000519 | 0.023486 |
| GO:0043488 | 0.000519 | 0.023486 |
| GO:0009913 | 0.000554 | 0.024722 |
| GO:0001933 | 0.000599 | 0.026437 |
| GO:0071482 | 0.000644 | 0.028056 |
| GO:0006357 | 0.000655 | 0.028101 |
| GO:0000079 | 0.000669 | 0.028101 |
| GO:1904029 | 0.000669 | 0.028101 |
| GO:0008544 | 0.000693 | 0.02877 |
| GO:0040007 | 0.000717 | 0.029419 |
| GO:0022402 | 0.000743 | 0.030129 |
| GO:0006950 | 0.000758 | 0.030396 |
| GO:1900739 | 0.000834 | 0.03271 |
| GO:1900740 | 0.000834 | 0.03271 |
| GO:0071158 | 0.000848 | 0.03287 |
| GO:0032269 | 0.000858 | 0.032918 |
| GO:0007050 | 0.000876 | 0.032997 |
| GO:0042771 | 0.000879 | 0.032997 |
| GO:0010556 | 0.000977 | 0.036285 |
| GO:0043903 | 0.000987 | 0.036285 |
| GO:0034349 | 0.001007 | 0.036608 |
| GO:0031326 | 0.001024 | 0.036862 |
| GO:0042326 | 0.001168 | 0.041617 |
| GO:0008630 | 0.00118 | 0.041637 |
| GO:0045892 | 0.001221 | 0.042507 |
| GO:0001844 | 0.001264 | 0.042507 |
| GO:0051204 | 0.001264 | 0.042507 |
| GO:0051205 | 0.001264 | 0.042507 |
| GO:0050789 | 0.001265 | 0.042507 |
| GO:0051248 | 0.001303 | 0.043375 |
| GO:0051254 | 0.001435 | 0.047304 |
| GO:1903507 | 0.001472 | 0.048101 |
| GO:1903901 | 0.001534 | 0.049636 |

## SI Table 10. Functional Enrichment GO terms between CellAge Senescence Promoter Genes and Oncogenes.

|  |  |  |
| --- | --- | --- |
| geneset | PValue | FDR |
| GO:0002684 | 1.12E-05 | 0.024944 |
| GO:0033554 | 2.75E-05 | 0.024944 |
| GO:0048732 | 3.66E-05 | 0.024944 |
| GO:0006950 | 4.51E-05 | 0.024944 |
| GO:0006461 | 5.69E-05 | 0.024944 |
| GO:0070271 | 5.69E-05 | 0.024944 |
| GO:0031571 | 8.35E-05 | 0.024944 |
| GO:0044783 | 8.35E-05 | 0.024944 |
| GO:0044819 | 8.35E-05 | 0.024944 |
| GO:0065003 | 9.09E-05 | 0.024944 |
| GO:0071822 | 0.000106 | 0.024944 |
| GO:0000075 | 0.000131 | 0.024944 |
| GO:0052547 | 0.000131 | 0.024944 |
| GO:0033993 | 0.000131 | 0.024944 |
| GO:0044773 | 0.000147 | 0.024944 |
| GO:0044774 | 0.000147 | 0.024944 |
| GO:0050851 | 0.000147 | 0.024944 |
| GO:0070482 | 0.000156 | 0.024944 |
| GO:2000045 | 0.000157 | 0.024944 |
| GO:0060341 | 0.000157 | 0.024944 |
| GO:0006952 | 0.000188 | 0.027623 |
| GO:0007093 | 0.000192 | 0.027623 |
| GO:0050678 | 0.000231 | 0.027623 |
| GO:1902806 | 0.000234 | 0.027623 |
| GO:0002682 | 0.000261 | 0.027623 |
| GO:0007267 | 0.000261 | 0.027623 |
| GO:0006955 | 0.00027 | 0.027623 |
| GO:0045087 | 0.000271 | 0.027623 |
| GO:0032879 | 0.000275 | 0.027623 |
| GO:0051130 | 0.000277 | 0.027623 |
| GO:0043933 | 0.000298 | 0.027623 |
| GO:0009411 | 0.000308 | 0.027623 |
| GO:1902807 | 0.000308 | 0.027623 |
| GO:2000134 | 0.000308 | 0.027623 |
| GO:0070201 | 0.000308 | 0.027623 |
| GO:0008285 | 0.000313 | 0.027623 |
| GO:0001666 | 0.000338 | 0.029039 |
| GO:0030154 | 0.000357 | 0.029812 |
| GO:0002429 | 0.000403 | 0.032018 |
| GO:0022409 | 0.000403 | 0.032018 |
| GO:0036293 | 0.000478 | 0.037019 |
| GO:0002253 | 0.000531 | 0.038298 |
| GO:0002757 | 0.000531 | 0.038298 |
| GO:0051249 | 0.000531 | 0.038298 |
| GO:0052548 | 0.000563 | 0.039753 |
| GO:0045944 | 0.000674 | 0.041146 |
| GO:0048513 | 0.000675 | 0.041146 |
| GO:0010468 | 0.000677 | 0.041146 |
| GO:0000077 | 0.000709 | 0.041146 |
| GO:0051259 | 0.000709 | 0.041146 |
| GO:0033138 | 0.000712 | 0.041146 |
| GO:0097190 | 0.000723 | 0.041146 |
| GO:1902580 | 0.000737 | 0.041146 |
| GO:1903037 | 0.000771 | 0.041146 |
| GO:0050878 | 0.00079 | 0.041146 |
| GO:0030162 | 0.000795 | 0.041146 |
| GO:0050673 | 0.000795 | 0.041146 |
| GO:0046903 | 0.000799 | 0.041146 |
| GO:0051128 | 0.000846 | 0.041146 |
| GO:0031570 | 0.000855 | 0.041146 |
| GO:0007166 | 0.00089 | 0.041146 |
| GO:0045930 | 0.000895 | 0.041146 |
| GO:0022407 | 0.000896 | 0.041146 |
| GO:0043903 | 0.000908 | 0.041146 |
| GO:0001934 | 0.000914 | 0.041146 |
| GO:0006810 | 0.000945 | 0.041146 |
| GO:0016043 | 0.000946 | 0.041146 |
| GO:0048869 | 0.000964 | 0.041146 |
| GO:0048731 | 0.001011 | 0.041146 |
| GO:0031325 | 0.001013 | 0.041146 |
| GO:0007050 | 0.001014 | 0.041146 |
| GO:0002768 | 0.001035 | 0.041146 |
| GO:0051251 | 0.001035 | 0.041146 |
| GO:0072657 | 0.001035 | 0.041146 |
| GO:0010165 | 0.001039 | 0.041146 |
| GO:1902578 | 0.001049 | 0.041146 |
| GO:0032501 | 0.001088 | 0.041146 |
| GO:0019219 | 0.00109 | 0.041146 |
| GO:0043901 | 0.001124 | 0.041146 |
| GO:0072332 | 0.001124 | 0.041146 |
| GO:1904031 | 0.001124 | 0.041146 |
| GO:0051704 | 0.00114 | 0.041146 |
| GO:0033135 | 0.001142 | 0.041146 |
| GO:0002694 | 0.001144 | 0.041146 |
| GO:0002764 | 0.001144 | 0.041146 |
| GO:0031401 | 0.001163 | 0.041146 |
| GO:0009605 | 0.001186 | 0.041146 |
| GO:0009416 | 0.001191 | 0.041146 |
| GO:0090304 | 0.001195 | 0.041146 |
| GO:0071840 | 0.001196 | 0.041146 |
| GO:0043281 | 0.001215 | 0.041146 |
| GO:1901991 | 0.001215 | 0.041146 |
| GO:0010033 | 0.001215 | 0.041146 |
| GO:0051252 | 0.00122 | 0.041146 |
| GO:0042127 | 0.00124 | 0.041146 |
| GO:0032880 | 0.001244 | 0.041146 |
| GO:0008283 | 0.001277 | 0.041266 |
| GO:0045786 | 0.001286 | 0.041266 |
| GO:0045785 | 0.001288 | 0.041266 |
| GO:0018130 | 0.001312 | 0.041266 |
| GO:0034654 | 0.001312 | 0.041266 |
| GO:0072594 | 0.001352 | 0.041964 |
| GO:0007275 | 0.001374 | 0.041964 |
| GO:0019438 | 0.001374 | 0.041964 |
| GO:1901988 | 0.001434 | 0.042557 |
| GO:1903039 | 0.001434 | 0.042557 |
| GO:2000116 | 0.001434 | 0.042557 |
| GO:0006351 | 0.001469 | 0.043091 |
| GO:0010604 | 0.001479 | 0.043091 |
| GO:0042327 | 0.001514 | 0.043712 |
| GO:0030857 | 0.00153 | 0.043781 |
| GO:0002696 | 0.001561 | 0.044263 |
| GO:0097659 | 0.00161 | 0.045057 |
| GO:0050778 | 0.001617 | 0.045057 |
| GO:1901362 | 0.001649 | 0.045547 |
| GO:0043900 | 0.001742 | 0.047285 |
| GO:0006366 | 0.001742 | 0.047285 |
| GO:0046889 | 0.00177 | 0.047418 |
| GO:0000082 | 0.001777 | 0.047418 |
| GO:0042060 | 0.001817 | 0.047729 |
| GO:0032774 | 0.001845 | 0.047729 |
| GO:0045184 | 0.001859 | 0.047729 |
| GO:0042981 | 0.001863 | 0.047729 |
| GO:0051234 | 0.00188 | 0.047729 |
| GO:0048584 | 0.001959 | 0.047729 |
| GO:0065008 | 0.001959 | 0.047729 |
| GO:0010467 | 0.001971 | 0.047729 |
| GO:0010562 | 0.001988 | 0.047729 |
| GO:0045937 | 0.001988 | 0.047729 |
| GO:0072331 | 0.002015 | 0.047729 |
| GO:0097193 | 0.002015 | 0.047729 |
| GO:0002220 | 0.002029 | 0.047729 |
| GO:0002223 | 0.002029 | 0.047729 |
| GO:0030073 | 0.002029 | 0.047729 |
| GO:0050852 | 0.002029 | 0.047729 |
| GO:0009628 | 0.002056 | 0.047843 |
| GO:0051171 | 0.002064 | 0.047843 |
| GO:0032270 | 0.002089 | 0.048076 |
| GO:0009611 | 0.002172 | 0.04963 |
| GO:0043067 | 0.002191 | 0.049709 |
| GO:0008015 | 0.002276 | 0.049899 |
| GO:0090150 | 0.002276 | 0.049899 |
| GO:0044843 | 0.002278 | 0.049899 |
| GO:0050867 | 0.002278 | 0.049899 |
| GO:1901990 | 0.002278 | 0.049899 |

## SI Table 11. Functional Enrichment GO terms between CellAge Senescence Inhibitor Genes and TSGs.

|  |  |  |
| --- | --- | --- |
| geneset | PValue | FDR |
| GO:1901701 | 1.67E-05 | 0.025629 |
| GO:0008585 | 1.70E-05 | 0.025629 |
| GO:0046545 | 2.24E-05 | 0.025629 |
| GO:1905269 | 2.91E-05 | 0.025629 |
| GO:0046660 | 3.72E-05 | 0.026199 |

## SI Table 12. Functional Enrichment GO terms between CellAge Senescence Inhibitor Genes and Oncogenes.

|  |  |  |
| --- | --- | --- |
| geneset | PValue | FDR |
| GO:0033554 | 4.92E-07 | 0.00116 |
| GO:1903507 | 8.98E-07 | 0.00116 |
| GO:1902679 | 1.10E-06 | 0.00116 |
| GO:0051253 | 1.49E-06 | 0.001176 |
| GO:0045934 | 4.26E-06 | 0.002694 |
| GO:0010558 | 8.00E-06 | 0.00421 |
| GO:0031327 | 9.52E-06 | 0.004296 |
| GO:0051172 | 1.13E-05 | 0.004464 |
| GO:0045892 | 1.38E-05 | 0.004602 |
| GO:0009890 | 1.46E-05 | 0.004602 |
| GO:0006355 | 2.63E-05 | 0.006721 |
| GO:2001020 | 2.92E-05 | 0.006721 |
| GO:0042127 | 3.07E-05 | 0.006721 |
| GO:1903506 | 3.19E-05 | 0.006721 |
| GO:2001141 | 3.19E-05 | 0.006721 |
| GO:0080135 | 3.51E-05 | 0.006935 |
| GO:0008283 | 3.74E-05 | 0.006939 |
| GO:2000112 | 4.12E-05 | 0.007235 |
| GO:0051252 | 5.28E-05 | 0.008777 |
| GO:2000113 | 6.04E-05 | 0.009083 |
| GO:1901701 | 6.21E-05 | 0.009083 |
| GO:0010556 | 6.33E-05 | 0.009083 |
| GO:0006351 | 6.75E-05 | 0.009264 |
| GO:0031326 | 7.14E-05 | 0.009264 |
| GO:0031324 | 7.35E-05 | 0.009264 |
| GO:0097659 | 7.63E-05 | 0.009264 |
| GO:0010605 | 9.00E-05 | 0.009927 |
| GO:0009889 | 9.06E-05 | 0.009927 |
| GO:0032774 | 9.14E-05 | 0.009927 |
| GO:0008284 | 9.43E-05 | 0.009927 |
| GO:0031648 | 9.96E-05 | 0.010147 |
| GO:0006357 | 0.00012 | 0.011831 |
| GO:0040007 | 0.000135 | 0.012961 |
| GO:0051171 | 0.000153 | 0.014023 |
| GO:0006974 | 0.000159 | 0.014023 |
| GO:0044271 | 0.000162 | 0.014023 |
| GO:0034614 | 0.000164 | 0.014023 |
| GO:0014855 | 0.000183 | 0.015013 |
| GO:0010468 | 0.000192 | 0.015013 |
| GO:0000122 | 0.000195 | 0.015013 |
| GO:0050678 | 0.000197 | 0.015013 |
| GO:0051240 | 0.0002 | 0.015013 |
| GO:0009636 | 0.000205 | 0.015018 |
| GO:0009892 | 0.000209 | 0.015018 |
| GO:0034599 | 0.00024 | 0.016865 |
| GO:0010629 | 0.000254 | 0.017464 |
| GO:0034645 | 0.000285 | 0.01887 |
| GO:0019219 | 0.00029 | 0.01887 |
| GO:0044703 | 0.000293 | 0.01887 |
| GO:0018130 | 0.000306 | 0.018974 |
| GO:0034654 | 0.000306 | 0.018974 |
| GO:0019438 | 0.000324 | 0.019666 |
| GO:0016070 | 0.000342 | 0.020387 |
| GO:0050673 | 0.000358 | 0.020948 |
| GO:0046622 | 0.000374 | 0.021489 |
| GO:0006325 | 0.00039 | 0.021519 |
| GO:0009059 | 0.000395 | 0.021519 |
| GO:0051094 | 0.000395 | 0.021519 |
| GO:0048523 | 0.000426 | 0.022301 |
| GO:1901362 | 0.000426 | 0.022301 |
| GO:0006366 | 0.000431 | 0.022301 |
| GO:0048589 | 0.000448 | 0.022841 |
| GO:0006950 | 0.000459 | 0.023028 |
| GO:0006282 | 0.000514 | 0.02495 |
| GO:0060419 | 0.000514 | 0.02495 |
| GO:0019953 | 0.000542 | 0.025625 |
| GO:0000060 | 0.000544 | 0.025625 |
| GO:0060485 | 0.000637 | 0.029572 |
| GO:0051239 | 0.000652 | 0.029829 |
| GO:0010604 | 0.000675 | 0.030467 |
| GO:0010467 | 0.000708 | 0.031084 |
| GO:0048518 | 0.000709 | 0.031084 |
| GO:0033158 | 0.000733 | 0.031704 |
| GO:0000302 | 0.000791 | 0.033746 |
| GO:0050793 | 0.00082 | 0.03395 |
| GO:0046677 | 0.000828 | 0.03395 |
| GO:0090344 | 0.000828 | 0.03395 |
| GO:0040008 | 0.000839 | 0.033978 |
| GO:0048754 | 0.000851 | 0.034012 |
| GO:0080134 | 0.000916 | 0.036143 |
| GO:0009888 | 0.000982 | 0.037973 |
| GO:0048519 | 0.000986 | 0.037973 |
| GO:0016569 | 0.001063 | 0.040434 |
| GO:0045995 | 0.001169 | 0.04396 |
| GO:0060421 | 0.001203 | 0.044181 |
| GO:2001022 | 0.001203 | 0.044181 |
| GO:0044249 | 0.001242 | 0.044931 |
| GO:0009893 | 0.00126 | 0.044931 |
| GO:0060560 | 0.001266 | 0.044931 |
| GO:0071236 | 0.001422 | 0.048801 |
| GO:0072074 | 0.001422 | 0.048801 |
| GO:0072075 | 0.001422 | 0.048801 |
| GO:0060562 | 0.001438 | 0.048821 |
| GO:0007517 | 0.001454 | 0.048849 |

## SI Table 13. PPI network results showing genes ranking in the top 1%, ranked according to appearance in multiple categories.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Degree** | **BC** | **CC** | **IC** | **Score** |
| EP300 | EP300 | EP300 | EP300 | 4 |
| MDM2 | MDM2 | MDM2 | MDM2 | 4 |
| CREBBP | CREBBP | CREBBP | CREBBP | 4 |
| SP1 | SP1 | SP1 | SP1 | 4 |
| TP53 | TP53 | TP53 |  | 3 |
| HDAC1 | HDAC1 | HDAC1 |  | 3 |
| BRCA1 | BRCA1 | BRCA1 |  | 3 |
| UBC | UBC | UBC |  | 3 |
| EGFR | EGFR | EGFR |  | 3 |
| AKT1 | AKT1 | AKT1 |  | 3 |
| ESR1 | ESR1 | ESR1 |  | 3 |
| AR | AR | AR |  | 3 |
| HDAC2 | HDAC2 | HDAC2 |  | 3 |
| HSP90AA1 | HSP90AA1 | HSP90AA1 |  | 3 |
| RB1 | RB1 | RB1 |  | 3 |
| MYC | MYC | MYC |  | 3 |
| UBE2I | UBE2I | UBE2I |  | 3 |
| CTNNB1 | CTNNB1 | CTNNB1 |  | 3 |
| CSNK2A1 | CSNK2A1 | CSNK2A1 |  | 3 |
| BTRC | BTRC |  | BTRC | 3 |
| PML | PML | PML |  | 3 |
| SMAD3 |  | SMAD3 | SMAD3 | 3 |
| BAG3 | BAG3 |  |  | 2 |
| SRC | SRC |  |  | 2 |
| CDK2 |  |  |  | 1 |
| HIST1H3A |  |  |  | 1 |
|  | TRIM28 |  |  | 1 |
|  | RUVBL2 |  |  | 1 |
|  | YAP1 |  |  | 1 |
|  |  | STUB1 |  | 1 |
|  |  | VCP |  | 1 |
|  |  | HSPA8 |  | 1 |
|  |  | RELA |  | 1 |
|  |  | VHL |  | 1 |
|  |  |  | CCND2 | 1 |
|  |  |  | EGR1 | 1 |
|  |  |  | CCND1 | 1 |
|  |  |  | CDKN2A | 1 |
|  |  |  | MAPK7 | 1 |
|  |  |  | CDK6 | 1 |
|  |  |  | DNMT1 | 1 |
|  |  |  | PIN1 | 1 |
|  |  |  | MAPK1 | 1 |
|  |  |  | SMARCC1 | 1 |
|  |  |  | CCND3 | 1 |
|  |  |  | CCAR2 | 1 |
|  |  |  | STAT3 | 1 |
|  |  |  | PCNA | 1 |
|  |  |  | ZBTB2 | 1 |
|  |  |  | CDKN2D | 1 |
|  |  |  | BCL11A | 1 |
|  |  |  | MDM4 | 1 |
|  |  |  | SIRT1 | 1 |
|  |  |  | PHB | 1 |

## SI Table 14. PPI Network Functional Enrichment Analysis. DAVID analysis of enriched clusters of related functional terms of the Protein-Protein Interaction (PPI) network. Clusters are ordered by enrichment score. The left column displays the database of origin of the enriched terms on the right.

|  |  |
| --- | --- |
| Module 1. Modularity score: 6.75 | |
| Cluster 1. Enrichment Score: 109.00 | |
| Database: | Terms: |
| GOTERM\_BP\_DIRECT | GO:0006351~transcription, DNA-templated |
| UP\_KEYWORDS | Transcription |
| UP\_KEYWORDS | Transcription regulation |
| Cluster 2. Enrichment Score: 61.44 | |
| Database: | Terms: |
| GOTERM\_BP\_DIRECT | GO:0006281~DNA repair |
| UP\_KEYWORDS | DNA damage |
| UP\_KEYWORDS | DNA repair |
| Cluster 3. Enrichment Score: 39.65 | |
| Database: | Terms: |
| GOTERM\_BP\_DIRECT | GO:0006468~protein phosphorylation |
| GOTERM\_MF\_DIRECT | GO:0004672~protein kinase activity |
| GOTERM\_MF\_DIRECT | GO:0005524~ATP binding |
| GOTERM\_MF\_DIRECT | GO:0004674~protein serine/threonine kinase activity |
| INTERPRO | IPR011009:Protein kinase-like domain |
| INTERPRO | IPR000719:Protein kinase, catalytic domain |
| INTERPRO | IPR017441:Protein kinase, ATP binding site |
| INTERPRO | IPR008271:Serine/threonine-protein kinase, active site |
| SMART | SM00220:S\_TKc |
| UP\_KEYWORDS | ATP-binding |
| UP\_KEYWORDS | Kinase |
| UP\_KEYWORDS | Serine/threonine-protein kinase |
| UP\_KEYWORDS | Nucleotide-binding |
| UP\_KEYWORDS | Transferase |
| UP\_SEQ\_FEATURE | nucleotide phosphate-binding region:ATP |
| UP\_SEQ\_FEATURE | domain:Protein kinase |
| UP\_SEQ\_FEATURE | binding site:ATP |
| UP\_SEQ\_FEATURE | active site:Proton acceptor |
| Cluster 4. Enrichment Score: 39.49 | |
| Database: | Terms: |
| GOTERM\_BP\_DIRECT | GO:0043161~proteasome-mediated ubiquitin-dependent protein catabolic process |
| GOTERM\_BP\_DIRECT | GO:0031145~anaphase-promoting complex-dependent catabolic process |
| GOTERM\_BP\_DIRECT | GO:0002223~stimulatory C-type lectin receptor signaling pathway |
| GOTERM\_BP\_DIRECT | GO:0000209~protein polyubiquitination |
| GOTERM\_BP\_DIRECT | GO:0051437~positive regulation of ubiquitin-protein ligase activity involved in regulation of mitotic cell cycle transition |
| GOTERM\_BP\_DIRECT | GO:0038095~Fc-epsilon receptor signaling pathway |
| GOTERM\_BP\_DIRECT | GO:0051436~negative regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle |
| GOTERM\_BP\_DIRECT | GO:0050852~T cell receptor signaling pathway |
| GOTERM\_BP\_DIRECT | GO:0000165~MAPK cascade |
| GOTERM\_BP\_DIRECT | GO:0038061~NIK/NF-kappaB signaling |
| GOTERM\_BP\_DIRECT | GO:0090090~negative regulation of canonical Wnt signaling pathway |
| GOTERM\_BP\_DIRECT | GO:0043488~regulation of mRNA stability |
| GOTERM\_BP\_DIRECT | GO:0006521~regulation of cellular amino acid metabolic process |
| GOTERM\_BP\_DIRECT | GO:0060071~Wnt signaling pathway, planar cell polarity pathway |
| GOTERM\_BP\_DIRECT | GO:0090263~positive regulation of canonical Wnt signaling pathway |
| GOTERM\_BP\_DIRECT | GO:0033209~tumor necrosis factor-mediated signaling pathway |
| GOTERM\_BP\_DIRECT | GO:0002479~antigen processing and presentation of exogenous peptide antigen via MHC class I, TAP-dependent |
| GOTERM\_CC\_DIRECT | GO:0000502~proteasome complex |
| KEGG\_PATHWAY | hsa03050:Proteasome |
| UP\_KEYWORDS | Proteasome |
| Cluster 5. Enrichment Score: 35.58 | |
| Database: | Terms: |
| GOTERM\_BP\_DIRECT | GO:0051301~cell division |
| GOTERM\_BP\_DIRECT | GO:0007067~mitotic nuclear division |
| UP\_KEYWORDS | Cell cycle |
| UP\_KEYWORDS | Cell division |
| UP\_KEYWORDS | Mitosis |

## SI Table 15. RNAseq Unweighted Co-expression Network Modules Functional Enrichment Analysis. The table displays the results of DAVID analysis of enriched clusters of related functional terms of the functional modules within the RNAseq unweighted co-expression network containing at least 34 nodes. Clusters are ordered by enrichment score. The left column displays the database of origin of the enriched terms on the right.

|  |  |
| --- | --- |
| Module 1. Modularity score: 764.04 | |
| Cluster 1. Enrichment Score: 5.98 | |
| Database: | Terms: |
| GOTERM\_BP\_DIRECT | GO:0007283~spermatogenesis |
| GOTERM\_BP\_DIRECT | GO:0030154~cell differentiation |
| GOTERM\_BP\_DIRECT | GO:0007275~multicellular organism development |
| UP\_KEYWORDS | Spermatogenesis |
| UP\_KEYWORDS | Differentiation |
| UP\_KEYWORDS | Developmental protein |
| Module 2. Modularity score: 514.91 | |
| Cluster 1. Enrichment Score: 38.59 | |
| Database: | Terms: |
| GOTERM\_CC\_DIRECT | GO:0030054~cell junction |
| UP\_KEYWORDS | Synapse |
| UP\_KEYWORDS | Cell junction |
| Module 3. Modularity score: 284.43 | |
| Cluster 1. Enrichment Score: 9.17 | |
| Database: | Terms: |
| GOTERM\_BP\_DIRECT | GO:0060048~cardiac muscle contraction |
| GOTERM\_BP\_DIRECT | GO:0030049~muscle filament sliding |
| GOTERM\_BP\_DIRECT | GO:0055010~ventricular cardiac muscle tissue morphogenesis |
| GOTERM\_BP\_DIRECT | GO:0002026~regulation of the force of heart contraction |
| GOTERM\_BP\_DIRECT | GO:0032781~positive regulation of ATPase activity |
| GOTERM\_BP\_DIRECT | GO:0006942~regulation of striated muscle contraction |
| GOTERM\_CC\_DIRECT | GO:0030017~sarcomere |
| GOTERM\_CC\_DIRECT | GO:0016459~myosin complex |
| KEGG\_PATHWAY | hsa05414:Dilated cardiomyopathy |
| KEGG\_PATHWAY | hsa04261:Adrenergic signaling in cardiomyocytes |
| KEGG\_PATHWAY | hsa05410:Hypertrophic cardiomyopathy (HCM) |
| KEGG\_PATHWAY | hsa04260:Cardiac muscle contraction |
| UP\_KEYWORDS | Cardiomyopathy |
| UP\_KEYWORDS | Muscle protein |
| UP\_KEYWORDS | Myosin |
| UP\_KEYWORDS | Motor protein |
| Module 4. Modularity score: 236.34 | |
| Cluster 1. Enrichment Score: 10.87 | |
| Database: | Terms: |
| GOTERM\_BP\_DIRECT | GO:0051301~cell division |
| GOTERM\_BP\_DIRECT | GO:0007067~mitotic nuclear division |
| UP\_KEYWORDS | Cell cycle |
| UP\_KEYWORDS | Mitosis |
| UP\_KEYWORDS | Cell division |
| Module 5. Modularity score: 168.824 | |
| Cluster 1. Enrichment Score: 24.74 | |
| Database: | Terms: |
| GOTERM\_CC\_DIRECT | GO:0005576~extracellular region |
| GOTERM\_CC\_DIRECT | GO:0005615~extracellular space |
| GOTERM\_CC\_DIRECT | GO:0070062~extracellular exosome |
| UP\_KEYWORDS | Secreted |
| UP\_KEYWORDS | Signal |
| UP\_KEYWORDS | Disulfide bond |
| UP\_KEYWORDS | Glycoprotein |
| UP\_SEQ\_FEATURE | signal peptide |
| UP\_SEQ\_FEATURE | disulfide bond |
| Module 6. Modularity score: 90.46 | |
| Cluster 1. Enrichment Score: 2.84 | |
| Database: | Terms: |
| INTERPRO | IPR002999:Tudor domain |
| SMART | SM00333:TUDOR |
| UP\_SEQ\_FEATURE | domain:Tudor |
| Module 7. Modularity score: 76.14 | |
| Cluster 1. Enrichment Score: 2.64 | |
| Database: | Terms: |
| GOTERM\_MF\_DIRECT | GO:0005524~ATP binding |
| INTERPRO | IPR027417:P-loop containing nucleoside triphosphate hydrolase |
| UP\_KEYWORDS | ATP-binding |
| UP\_KEYWORDS | Nucleotide-binding |
| UP\_SEQ\_FEATURE | nucleotide phosphate-binding region:ATP |
| Module 8. Modularity score: 69.05 | |
| Cluster 1. Enrichment Score: 5.25 | |
| Database: | Terms: |
| GOTERM\_BP\_DIRECT | GO:0006814~sodium ion transport |
| GOTERM\_BP\_DIRECT | GO:0055085~transmembrane transport |
| GOTERM\_BP\_DIRECT | GO:0035725~sodium ion transmembrane transport |
| GOTERM\_CC\_DIRECT | GO:0005887~integral component of plasma membrane |
| GOTERM\_MF\_DIRECT | GO:0005215~transporter activity |
| UP\_KEYWORDS | Symport |
| UP\_KEYWORDS | Ion transport |
| UP\_KEYWORDS | Sodium transport |
| UP\_KEYWORDS | Sodium |
| Module 9. Modularity score: 58.92 | |
| Cluster 1. Enrichment Score: 2.30 | |
| Database: | Terms: |
| GOTERM\_BP\_DIRECT | GO:0006281~DNA repair |
| GOTERM\_BP\_DIRECT | GO:0006310~DNA recombination |
| UP\_KEYWORDS | DNA damage |
| UP\_KEYWORDS | DNA repair |
| UP\_KEYWORDS | DNA recombination |
| Module 10. Modularity score: 55.918 | |
| Cluster 1. Enrichment Score: 2.99 | |
| Database: | Terms: |
| UP\_KEYWORDS | Mitochondrion |
| UP\_KEYWORDS | Transit peptide |
| UP\_SEQ\_FEATURE | transit peptide:Mitochondrion |
| Module 11. Modularity score: 33.545 | |
| Cluster 1. Enrichment Score: 6.46 | |
| Database: | Terms: |
| GOTERM\_BP\_DIRECT | GO:0006355~regulation of transcription, DNA-templated |
| GOTERM\_BP\_DIRECT | GO:0006351~transcription, DNA-templated |
| GOTERM\_CC\_DIRECT | GO:0005634~nucleus |
| UP\_KEYWORDS | Transcription regulation |
| UP\_KEYWORDS | Transcription |
| UP\_KEYWORDS | Nucleus |
| UP\_KEYWORDS | DNA-binding |
| Module 12. Modularity score: 31.01 | |
| Cluster 1. Enrichment Score: 2.08 | |
| Database: | Terms: |
| GOTERM\_BP\_DIRECT | GO:0015031~protein transport |
| UP\_KEYWORDS | Protein transport |
| UP\_KEYWORDS | Transport |
| Module 13. Modularity score: 10.54 | |
| Cluster 1. Enrichment Score: 13.79 | |
| Database: | Terms: |
| GOTERM\_BP\_DIRECT | GO:0006120~mitochondrial electron transport, NADH to ubiquinone |
| GOTERM\_BP\_DIRECT | GO:1902600~hydrogen ion transmembrane transport |
| GOTERM\_BP\_DIRECT | GO:0032981~mitochondrial respiratory chain complex I assembly |
| GOTERM\_CC\_DIRECT | GO:0005743~mitochondrial inner membrane |
| GOTERM\_CC\_DIRECT | GO:0005747~mitochondrial respiratory chain complex I |
| GOTERM\_MF\_DIRECT | GO:0008137~NADH dehydrogenase (ubiquinone) activity |
| KEGG\_PATHWAY | hsa00190:Oxidative phosphorylation |
| KEGG\_PATHWAY | hsa05016:Huntington's disease |
| KEGG\_PATHWAY | hsa05012:Parkinson's disease |
| KEGG\_PATHWAY | hsa05010:Alzheimer's disease |
| KEGG\_PATHWAY | hsa04932:Non-alcoholic fatty liver disease (NAFLD) |
| KEGG\_PATHWAY | hsa01100:Metabolic pathways |
| KEGG\_PATHWAY | hsa04260:Cardiac muscle contraction |
| UP\_KEYWORDS | Mitochondrion |
| UP\_KEYWORDS | Mitochondrion inner membrane |
| UP\_KEYWORDS | Respiratory chain |
| UP\_KEYWORDS | Electron transport |
| UP\_KEYWORDS | Transport |
| UP\_KEYWORDS | Membrane |
| Module 14. Modularity score: 6.16 | |
| Cluster 1. Enrichment Score: 3.68 | |
| Database: | Terms: |
| BIOCARTA | h\_ahspPathway:Hemoglobin's Chaperone |
| GOTERM\_BP\_DIRECT | GO:0006783~heme biosynthetic process |
| KEGG\_PATHWAY | hsa00860:Porphyrin and chlorophyll metabolism |
| KEGG\_PATHWAY | hsa01100:Metabolic pathways |
| UP\_KEYWORDS | Heme biosynthesis |
| Module 15. Modularity score: 3.20 | |
| Cluster 1. Enrichment Score: 21.85 | |
| Database: | Terms: |
| GOTERM\_BP\_DIRECT | GO:0045087~innate immune response |
| UP\_KEYWORDS | Immunity |
| UP\_KEYWORDS | Innate immunity |

## SI Table 16. RNA-Seq Co-expression Network Functional Enrichment Analysis. The table displays the results of DAVID analysis of enriched clusters of the two largest clusters identified from the network, plus the cluster comprising the highest proportion of CellAge genes. Functional clusters identified using DAVID are ordered by enrichment score. The left column displays the Ensembl Id and the term is on the right.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Cluster 1 - 460 Nodes (17 CellAge nodes)** | | | | |
| **DAVID Annotation Cluster 1: Enrichment Score: 10.87** | | | | |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| UP\_KEYWORDS | Cell cycle | 50 | 6E-14 | 1.8E-11 |
| UP\_KEYWORDS | Mitosis | 30 | 1E-12 | 1E-10 |
| UP\_KEYWORDS | Cell division | 36 | 1.9E-12 | 1.4E-10 |
| GOTERM\_BP\_DIRECT | cell division | 34 | 9.8E-12 | 1.5E-08 |
| GOTERM\_BP\_DIRECT | mitotic nuclear division | 22 | 3.9E-07 | 0.00029 |
| **DAVID Annotation Cluster 2: Enrichment Score: 5.89** | | | | |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| UP\_KEYWORDS | DNA repair | 24 | 1.6E-07 | 0.000007 |
| UP\_KEYWORDS | DNA damage | 26 | 3.3E-07 | 0.000011 |
| GOTERM\_BP\_DIRECT | DNA repair | 18 | 3.9E-05 | 0.0096 |
| **DAVID Annotation Cluster 3: Enrichment Score: 4.66** | |  |  |  |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| UP\_KEYWORDS | Centromere | 17 | 6.2E-08 | 0.0000031 |
| UP\_KEYWORDS | Chromosome | 27 | 1E-06 | 0.000031 |
| GOTERM\_BP\_DIRECT | sister chromatid cohesion | 13 | 5E-06 | 0.0025 |
| UP\_KEYWORDS | Kinetochore | 11 | 6.7E-05 | 0.0013 |
| GOTERM\_CC\_DIRECT | condensed chromosome kinetochore | 10 | 0.00014 | 0.0098 |
| GOTERM\_CC\_DIRECT | kinetochore | 6 | 0.035 | 0.48 |
| **DAVID Annotation Cluster 4: Enrichment Score: 3.46** | |  |  |  |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| SMART | CYCLIN | 8 | 0.000011 | 0.00093 |
| SMART | SM01332 | 6 | 0.000034 | 0.0019 |
| INTERPRO | Cyclin, C-terminal domain | 6 | 0.000035 | 0.013 |
| INTERPRO | Cyclin-like | 8 | 0.000047 | 0.0086 |
| INTERPRO | Cyclin, N-terminal | 7 | 0.00009 | 0.013 |
| KEGG\_PATHWAY | Progesterone-mediated oocyte maturation | 9 | 0.0002 | 0.011 |
| UP\_KEYWORDS | Cyclin | 7 | 0.00022 | 0.0039 |
| KEGG\_PATHWAY | p53 signaling pathway | 4 | 0.13 | 0.79 |
| KEGG\_PATHWAY | FoxO signaling pathway | 5 | 0.24 | 0.9 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Cluster 2 - 450 Nodes (19 CellAge nodes)** | |  |  |  |
| **DAVID Annotation Cluster 1: Enrichment Score: 21.85** | |  |  |  |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| UP\_KEYWORDS | Immunity | 65 | 9.4E-32 | 2.5E-29 |
| UP\_KEYWORDS | Innate immunity | 37 | 2.7E-19 | 3.7E-17 |
| GOTERM\_BP\_DIRECT | innate immune response | 45 | 1.1E-16 | 7.4E-14 |
| **DAVID Annotation Cluster 2: Enrichment Score: 8.71** | |  |  |  |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| UP\_KEYWORDS | SH3 domain | 24 | 2E-10 | 8.8E-09 |
| INTERPRO | Src homology-3 domain | 24 | 8.1E-10 | 0.00000028 |
| UP\_SEQ\_FEATURE | domain:SH3 | 21 | 1.2E-09 | 0.00000078 |
| SMART | SH3 | 23 | 7.7E-08 | 0.0000075 |
| **DAVID Annotation Cluster 3: Enrichment Score: 7.65** | |  |  |  |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| KEGG\_PATHWAY | Malaria | 13 | 7.6E-09 | 0.00000033 |
| KEGG\_PATHWAY | NF-kappa B signaling pathway | 16 | 1.7E-08 | 0.00000059 |
| GOTERM\_BP\_DIRECT | positive regulation of NF-kappaB transcription factor activity | 17 | 8.5E-08 | 0.000012 |
| **DAVID Annotation Cluster 4: Enrichment Score: 6.65** | |  |  |  |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| UP\_KEYWORDS | Immunoglobulin domain | 43 | 4.9E-13 | 3.3E-11 |
| INTERPRO | Immunoglobulin-like fold | 56 | 1E-10 | 0.00000007 |
| INTERPRO | Immunoglobulin-like domain | 47 | 1.5E-09 | 0.00000035 |
| INTERPRO | Immunoglobulin subtype | 36 | 2.4E-09 | 0.00000042 |
| UP\_SEQ\_FEATURE | domain:Ig-like C2-type 1 | 19 | 0.00000039 | 0.000055 |
| UP\_SEQ\_FEATURE | domain:Ig-like C2-type 2 | 19 | 0.00000042 | 0.000053 |
| SMART | IG | 36 | 0.0000005 | 0.000032 |
| INTERPRO | Immunoglobulin V-set | 21 | 0.0012 | 0.038 |
| INTERPRO | Immunoglobulin subtype 2 | 15 | 0.0016 | 0.043 |
| SMART | IGc2 | 15 | 0.011 | 0.15 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Cluster 17 - 51 Nodes (10 CellAge)** | | | | |
| **DAVID Annotation Cluster 1 - Enrichment Score: 4.9** | |  |  |  |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| UP\_SEQ\_FEATURE | signal peptide | 27 | 0.00000001 | 0.0000025 |
| UP\_KEYWORDS | Signal | 27 | 0.00000059 | 0.000078 |
| UP\_KEYWORDS | Glycoprotein | 27 | 0.0000035 | 0.00016 |
| UP\_SEQ\_FEATURE | glycosylation site:N-linked (GlcNAc...) | 25 | 0.000021 | 0.0017 |
| UP\_KEYWORDS | Disulfide bond | 18 | 0.0022 | 0.026 |
| UP\_SEQ\_FEATURE | disulfide bond | 16 | 0.0039 | 0.13 |
| **DAVID Annotation Cluster 2 - Enrichment Score: 3.19** | |  |  |  |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| KEGG\_PATHWAY | Focal adhesion | 8 | 0.00000029 | 0.000019 |
| KEGG\_PATHWAY | ECM-receptor interaction | 3 | 0.019 | 0.27 |
| KEGG\_PATHWAY | PI3K-Akt signaling pathway | 4 | 0.05 | 0.49 |
| **DAVID Annotation Cluster 3 - Enrichment Score: 3.01** | |  |  |  |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| GOTERM\_BP\_DIRECT | cell adhesion | 8 | 0.0002 | 0.043 |
| UP\_KEYWORDS | Cell adhesion | 7 | 0.001 | 0.023 |
| GOTERM\_BP\_DIRECT | positive regulation of cell-substrate adhesion | 3 | 0.0046 | 0.4 |
| **DAVID Annotation Cluster 4 - Enrichment Score: 2.98** | |  |  |  |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| INTERPRO | Insulin-like growth factor binding protein, N-terminal | 6 | 0.000032 | 0.0042 |
| UP\_SEQ\_FEATURE | domain:IGFBP N-terminal | 3 | 0.0011 | 0.053 |
| INTERPRO | Insulin-like growth factor-binding protein, IGFBP | 3 | 0.0013 | 0.054 |
| SMART | IB | 3 | 0.0015 | 0.029 |
| GOTERM\_BP\_DIRECT | regulation of cell growth | 3 | 0.019 | 0.71 |
| **DAVID Annotation Cluster 5 - Enrichment Score: 2.91** | |  |  |  |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| GOTERM\_CC\_DIRECT | proteinaceous extracellular matrix | 7 | 0.000079 | 0.0011 |
| UP\_SEQ\_FEATURE | domain:VWFC | 3 | 0.00091 | 0.053 |
| INTERPRO | von Willebrand factor, type C | 3 | 0.0052 | 0.13 |
| SMART | VWC | 3 | 0.0061 | 0.078 |
| **DAVID Annotation Cluster 6 - Enrichment Score: 2.52** | |  |  |  |
| **Database** | **Term** | **Count** | **P\_Value** | **Benjamini** |
| KEGG\_PATHWAY | Focal adhesion | 8 | 0.00000029 | 0.000019 |
| KEGG\_PATHWAY | Proteoglycans in cancer | 5 | 0.0012 | 0.038 |
| GOTERM\_CC\_DIRECT | cytoplasmic vesicle | 5 | 0.0036 | 0.03 |
| KEGG\_PATHWAY | Bacterial invasion of epithelial cells | 3 | 0.015 | 0.28 |
| GOTERM\_CC\_DIRECT | intracellular | 7 | 0.15 | 0.48 |
| GOTERM\_MF\_DIRECT | protein kinase binding | 3 | 0.28 | 0.95 |

## SI Table 17. CellAge Functional Enrichment Analysis. The table displays the results of DAVID analysis of enriched clusters of related functional terms. Clusters are ordered by enrichment score. The left column displays the database of origin of the enriched terms on the right.

|  |  |
| --- | --- |
| Cluster 1. Enrichment Score: 24.69 | |
| Database | Terms |
| GOTERM\_BP\_DIRECT | GO:0006468~protein phosphorylation |
| GOTERM\_MF\_DIRECT | GO:0004674~protein serine/threonine kinase activity |
| GOTERM\_MF\_DIRECT | GO:0004672~protein kinase activity |
| GOTERM\_MF\_DIRECT | GO:0005524~ATP binding |
| INTERPRO | IPR011009:Protein kinase-like domain |
| INTERPRO | IPR000719:Protein kinase, catalytic domain |
| INTERPRO | IPR017441:Protein kinase, ATP binding site |
| INTERPRO | IPR008271:Serine/threonine-protein kinase, active site |
| SMART | SM00220:S\_TKc |
| UP\_KEYWORDS | Kinase |
| UP\_KEYWORDS | Serine/threonine-protein kinase |
| UP\_KEYWORDS | Transferase |
| UP\_KEYWORDS | ATP-binding |
| UP\_KEYWORDS | Nucleotide-binding |
| UP\_SEQ\_FEATURE | binding site:ATP |
| UP\_SEQ\_FEATURE | domain:Protein kinase |
| UP\_SEQ\_FEATURE | active site:Proton acceptor |
| UP\_SEQ\_FEATURE | nucleotide phosphate-binding region:ATP |
| Cluster 2. Enrichment Score: 14.75 | |
| Database | Terms |
| GOTERM\_BP\_DIRECT | GO:0000122~negative regulation of transcription from RNA polymerase II promoter |
| GOTERM\_BP\_DIRECT | GO:0006351~transcription, DNA-templated |
| UP\_KEYWORDS | Transcription regulation |
| UP\_KEYWORDS | Transcription |
| UP\_KEYWORDS | Activator |
| Cluster 3. Enrichment Score: 8.33 | |
| Database | Terms |
| GOTERM\_BP\_DIRECT | GO:0006366~transcription from RNA polymerase II promoter |
| GOTERM\_MF\_DIRECT | GO:0003700~transcription factor activity, sequence-specific DNA binding |
| GOTERM\_MF\_DIRECT | GO:0043565~sequence-specific DNA binding |
| GOTERM\_MF\_DIRECT | GO:0003677~DNA binding |
| UP\_KEYWORDS | DNA-binding |
| Cluster 4. Enrichment Score: 5.55 | |
| Database | Terms |
| GOTERM\_BP\_DIRECT | GO:0006281~DNA repair |
| UP\_KEYWORDS | DNA damage |
| UP\_KEYWORDS | DNA repair |
| Cluster 5. Enrichment Score: 5.44 | |
| Database | Terms |
| BBID | 94.E2F\_transcriptional\_activity\_cell\_cycle |
| BBID | 26.cyclin-CDK\_complexes |
| BBID | 1.RBphosphoE2F |
| BIOCARTA | h\_g1Pathway:Cell Cycle: G1/S Check Point |
| BIOCARTA | h\_cellcyclePathway:Cyclins and Cell Cycle Regulation |
| BIOCARTA | h\_raccycdPathway:Influence of Ras and Rho proteins on G1 to S Transition |
| BIOCARTA | h\_mapkPathway:MAPKinase Signaling Pathway |
| BIOCARTA | h\_p53Pathway:p53 Signaling Pathway |
| BIOCARTA | h\_bArrestin-srcPathway:Roles of ?-arrestin-dependent Recruitment of Src Kinases in GPCR Signaling |
| BIOCARTA | h\_erkPathway:Erk1/Erk2 Mapk Signaling pathway |
| GOTERM\_BP\_DIRECT | GO:0006977~DNA damage response, signal transduction by p53 class mediator resulting in cell cycle arrest |
| GOTERM\_BP\_DIRECT | GO:0000082~G1/S transition of mitotic cell cycle |
| GOTERM\_CC\_DIRECT | GO:0000307~cyclin-dependent protein kinase holoenzyme complex |
| KEGG\_PATHWAY | hsa05219:Bladder cancer |
| KEGG\_PATHWAY | hsa05220:Chronic myeloid leukemia |
| KEGG\_PATHWAY | hsa05161:Hepatitis B |
| KEGG\_PATHWAY | hsa04110:Cell cycle |
| KEGG\_PATHWAY | hsa05223:Non-small cell lung cancer |
| KEGG\_PATHWAY | hsa05214:Glioma |
| KEGG\_PATHWAY | hsa04115:p53 signaling pathway |
| KEGG\_PATHWAY | hsa05218:Melanoma |
| KEGG\_PATHWAY | hsa05205:Proteoglycans in cancer |
| KEGG\_PATHWAY | hsa04068:FoxO signaling pathway |
| KEGG\_PATHWAY | hsa05200:Pathways in cancer |
| KEGG\_PATHWAY | hsa05221:Acute myeloid leukemia |
| KEGG\_PATHWAY | hsa04917:Prolactin signaling pathway |
| KEGG\_PATHWAY | hsa05215:Prostate cancer |
| KEGG\_PATHWAY | hsa05213:Endometrial cancer |
| KEGG\_PATHWAY | hsa05212:Pancreatic cancer |
| KEGG\_PATHWAY | hsa04550:Signaling pathways regulating pluripotency of stem cells |
| KEGG\_PATHWAY | hsa04664:Fc epsilon RI signaling pathway |
| KEGG\_PATHWAY | hsa05203:Viral carcinogenesis |
| KEGG\_PATHWAY | hsa04012:ErbB signaling pathway |
| KEGG\_PATHWAY | hsa04660:T cell receptor signaling pathway |
| KEGG\_PATHWAY | hsa04722:Neurotrophin signaling pathway |
| KEGG\_PATHWAY | hsa04010:MAPK signaling pathway |
| KEGG\_PATHWAY | hsa05230:Central carbon metabolism in cancer |
| KEGG\_PATHWAY | hsa05160:Hepatitis C |
| KEGG\_PATHWAY | hsa04919:Thyroid hormone signaling pathway |
| KEGG\_PATHWAY | hsa05216:Thyroid cancer |
| KEGG\_PATHWAY | hsa04370:VEGF signaling pathway |
| KEGG\_PATHWAY | hsa04380:Osteoclast differentiation |
| KEGG\_PATHWAY | hsa05211:Renal cell carcinoma |
| KEGG\_PATHWAY | hsa04914:Progesterone-mediated oocyte maturation |
| KEGG\_PATHWAY | hsa04912:GnRH signaling pathway |
| KEGG\_PATHWAY | hsa05210:Colorectal cancer |
| KEGG\_PATHWAY | hsa04151:PI3K-Akt signaling pathway |
| KEGG\_PATHWAY | hsa04915:Estrogen signaling pathway |
| KEGG\_PATHWAY | hsa05222:Small cell lung cancer |
| KEGG\_PATHWAY | hsa05145:Toxoplasmosis |
| KEGG\_PATHWAY | hsa04062:Chemokine signaling pathway |
| KEGG\_PATHWAY | hsa04662:B cell receptor signaling pathway |
| KEGG\_PATHWAY | hsa04510:Focal adhesion |
| KEGG\_PATHWAY | hsa04015:Rap1 signaling pathway |
| KEGG\_PATHWAY | hsa04910:Insulin signaling pathway |
| KEGG\_PATHWAY | hsa04071:Sphingolipid signaling pathway |
| KEGG\_PATHWAY | hsa05231:Choline metabolism in cancer |
| KEGG\_PATHWAY | hsa04666:Fc gamma R-mediated phagocytosis |
| KEGG\_PATHWAY | hsa04921:Oxytocin signaling pathway |
| KEGG\_PATHWAY | hsa04650:Natural killer cell mediated cytotoxicity |
| KEGG\_PATHWAY | hsa04730:Long-term depression |
| KEGG\_PATHWAY | hsa04022:cGMP-PKG signaling pathway |
| KEGG\_PATHWAY | hsa04024:cAMP signaling pathway |
| UP\_KEYWORDS | Cyclin |

## SI Table 18. Network: Microarray unweighted co-expression network.

|  |
| --- |
| Cluster 1. Enrichment Score: 54.94 Functional Enrichment Analysis |

|  |  |
| --- | --- |
| Database:  GOTERM\_BP\_DIRECT  GOTERM\_BP\_DIRECT  UP\_KEYWORDS  UP\_KEYWORDS  UP\_KEYWORDS | Terms:  GO:0051301~cell division  GO:0007067~mitotic nuclear division  Cell cycle  Cell division  Mitosis |
| Cluster 2. Enrichment Score: 33.43 | |
| Database:  GOTERM\_BP\_DIRECT  GOTERM\_CC\_DIRECT  GOTERM\_CC\_DIRECT  UP\_KEYWORDS  UP\_KEYWORDS  UP\_KEYWORDS | Terms:  GO:0007062~sister chromatid cohesion  GO:0000777~condensed chromosome kinetochore  GO:0000776~kinetochore  Chromosome  Centromere  Kinetochore |
| Cluster 3. Enrichment Score: 30.73 | |
| Database:  GOTERM\_BP\_DIRECT  UP\_KEYWORDS  UP\_KEYWORDS | Terms:  GO:0006281~DNA repair  DNA repair  DNA damage |
| Cluster 4. Enrichment Score: 26.86 | |
| Database:  GOTERM\_MF\_DIRECT  INTERPRO  UP\_KEYWORDS  UP\_KEYWORDS  UP\_SEQ\_FEATURE | Terms:  GO:0005524~ATP binding  IPR027417:P-loop containing nucleoside triphosphate hydrolase  ATP-binding  Nucleotide-binding  nucleotide phosphate-binding region:ATP |
| Cluster 5. Enrichment Score: 11.19 | |
| Database:  GOTERM\_MF\_DIRECT  GOTERM\_MF\_DIRECT  INTERPRO  INTERPRO  INTERPRO  INTERPRO  SMART  SMART  UP\_KEYWORDS  UP\_SEQ\_FEATURE  UP\_SEQ\_FEATURE  UP\_SEQ\_FEATURE | Terms:  GO:0004386~helicase activity  GO:0004004~ATP-dependent RNA helicase activity  IPR014001:Helicase, superfamily 1/2, ATP-binding domain  IPR001650:Helicase, C-terminal  IPR011545:DNA/RNA helicase, DEAD/DEAH box type, N-terminal  IPR000330:SNF2-related  SM00487:DEXDc  SM00490:HELICc  Helicase  domain:Helicase C-terminal  domain:Helicase ATP-binding  short sequence motif:DEAH box |

## SI Table 19. Microarray Unweighted Co-expression Network Modules Functional Enrichment Analysis

|  |  |
| --- | --- |
|  | |
| Module 1. Modularity score: 8192.0  Cluster 1. Enrichment Score: 15.01 | |
| Database:  GOTERM\_MF\_DIRECT  INTERPRO  INTERPRO  INTERPRO  INTERPRO  SMART  UP\_KEYWORDS  UP\_SEQ\_FEATURE | Terms:  GO:0043565~sequence-specific DNA binding  IPR017970:Homeobox, conserved site  IPR001356:Homeodomain  IPR009057:Homeodomain-like  IPR020479:Homeodomain, metazoa  SM00389:HOX  Homeobox  DNA-binding region:Homeobox |
| Cluster 2. Enrichment Score: 6.82 | |
| Database:  GOTERM\_BP\_DIRECT  GOTERM\_BP\_DIRECT  GOTERM\_CC\_DIRECT  GOTERM\_MF\_DIRECT  UP\_KEYWORDS  UP\_KEYWORDS  UP\_KEYWORDS  UP\_KEYWORDS | Terms:  GO:0006351~transcription, DNA-templated  GO:0006355~regulation of transcription, DNA-templated  GO:0005634~nucleus  GO:0003677~DNA binding  DNA-binding  Transcription regulation  Transcription  Nucleus |
| Cluster 3. Enrichment Score: 6.34 | |
| Database:  GOTERM\_MF\_DIRECT  INTERPRO  SMART  UP\_SEQ\_FEATURE  UP\_SEQ\_FEATURE | Terms:  GO:0046983~protein dimerization activity  IPR011598:Myc-type, basic helix-loop-helix (bHLH) domain  SM00353:HLH  domain:Helix-loop-helix motif  DNA-binding region:Basic motif |
| Module 2. Modularity score: 319.44  Cluster 1. Enrichment Score: 71.61 | |
| Database:  GOTERM\_BP\_DIRECT  GOTERM\_BP\_DIRECT  UP\_KEYWORDS  UP\_KEYWORDS  UP\_KEYWORDS | Terms:  GO:0051301~cell division  GO:0007067~mitotic nuclear division  Cell cycle  Cell division  Mitosis |
| Cluster 2. Enrichment Score: 45.1 | |
| Database:  GOTERM\_BP\_DIRECT  GOTERM\_CC\_DIRECT  GOTERM\_CC\_DIRECT  UP\_KEYWORDS  UP\_KEYWORDS  UP\_KEYWORDS | Terms:  GO:0007062~sister chromatid cohesion  GO:0000777~condensed chromosome kinetochore  GO:0000776~kinetochore  Chromosome  Centromere  Kinetochore |
| Cluster 3. Enrichment Score: 42.58 | |
| Database:  GOTERM\_BP\_DIRECT  UP\_KEYWORDS  UP\_KEYWORDS | Terms:  GO:0006281~DNA repair  DNA damage  DNA repair |
| Module 3. Modularity score: 318.5  Cluster 1. Enrichment Score: 20.72 | |
| Database:  GOTERM\_BP\_DIRECT  GOTERM\_BP\_DIRECT  GOTERM\_BP\_DIRECT  GOTERM\_MF\_DIRECT  UP\_KEYWORDS  UP\_KEYWORDS  UP\_KEYWORDS  UP\_KEYWORDS | Terms:  GO:0051607~defense response to virus  GO:0009615~response to virus  GO:0045087~innate immune response  GO:0003725~double-stranded RNA binding  Antiviral defense  Innate immunity  Immunity  RNA-binding |
| Cluster 2. Enrichment Score: 10.46 | |
| Database:  KEGG\_PATHWAY  KEGG\_PATHWAY  KEGG\_PATHWAY  KEGG\_PATHWAY  UP\_SEQ\_FEATURE | Terms:  hsa05164:Influenza A  hsa05168:Herpes simplex infection  hsa05162:Measles  hsa05160:Hepatitis C  mutagenesis site |
| Cluster 3. Enrichment Score: 6.13 | |
| Database:  KEGG\_PATHWAY  UP\_KEYWORDS  UP\_KEYWORDS  UP\_KEYWORDS  UP\_SEQ\_FEATURE | Terms:  hsa05168:Herpes simplex infection  Host-virus interaction  Ubl conjugation  Isopeptide bond  mutagenesis site |

## SI Table 22. Genes chosen for experimental validation, justification for choice, senescence morphology score, and senescence pathway activated. Genes in red activated both the p21 and the p16 pathway, and altered at least one phenotype towards senescence morphology (i.e. direction of change similar to CBX7 siRNA). Senescence morphology score calculated based on the sum of the number of morphological features that match senescence morphology with a Z-score of 1 or more, where each feature adds 1 to the morphology score (cell senescence phenotype is decreased cell number, increased cell area, increased nuclear area, and increased nuclear elongation, for a maximum score of 4 if all the cell features match senescence morphology).

|  |  |  |  |
| --- | --- | --- | --- |
| Gene | Justification | Senescence Morphology Score | Senescence Pathway |
| C9orf40 | Top co-expressed with CellAge senescence inhibitors | 3 | p21 |
| CAPRIN1 | Top co-expressed with CellAge senescence inhibitors | 4 | p21, p16 |
| CDC25A | Top co-expressed with CellAge senescence inhibitors | 2 | p21, p16 |
| CDCA4 | Top co-expressed with CellAge senescence inhibitors | 4 | p21 |
| CENPW | Co-expressed with CellAge SISP inhibitors, Underexpressed in RS | 1 | – |
| CKAP2 | Top co-expressed with CellAge senescence inhibitors | 2 | – |
| GTF3C4 | Top co-expressed with CellAge senescence inhibitors | 4 | p21 |
| HAUS4 | Co-expressed with CellAge SISP inhibitors, Underexpressed in RS | 4 | p21, p16 |
| HAUS8 | Co-expressed with CellAge SISP inhibitors, Underexpressed in RS | 2 | p21 |
| HNRNPAB | Top co-expressed with CellAge senescence inhibitors | 1 | – |
| IMMT | Top co-expressed with CellAge senescence inhibitors | 2 | p21 |
| MCM7 | Top co-expressed with CellAge senescence inhibitors | 3 | p21 |
| MRPS9 | Co-expressed with CellAge SISP inhibitors, Underexpressed in RS | 0 | – |
| MTHFD2 | Top co-expressed with CellAge senescence inhibitors | 2 | p21 |
| MYBL2 | Top co-expressed with CellAge senescence inhibitors | 4 | p21, p16 |
| NEK2 | Top co-expressed with CellAge senescence inhibitors | 2 | p21 |
| NIPA2 | Top co-expressed with CellAge senescence inhibitors | 3 | p21 |
| NOA1 | Top co-expressed with CellAge senescence inhibitors | 1 | – |
| NUP153 | Top co-expressed with CellAge senescence inhibitors | 2 | p21 |
| NUSAP1 | Top co-expressed with CellAge senescence inhibitors | 1 | p16 |
| RMI1 | Top co-expressed with CellAge senescence inhibitors | 2 | – |
| SMC4 | Top candidate from microarray network analyses, underexpressed in RS | 3 | p21, p16 |
| SPAG5 | Top co-expressed with CellAge senescence inhibitors | 4 | p21, p16 |
| TCEB3 | Top co-expressed with CellAge senescence inhibitors | 3 | p21 |
| VRK1 | Co-expressed with CellAge SISP inhibitors, Underexpressed in RS | 0 | – |
| WDR5 | Top co-expressed with CellAge senescence inhibitors | 2 | p21 |

## SI Table 23. siRNA Z-scores for every category.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Cell number** | **Cell Area** | **Nuclear Area** | **Nuclear Elongation** | **Cellular p16 intensity** | **Nuclear p21 intensity** |
| **siGLO** | 0 | 0 | 0 | 0 | 0 | 0 |
| **CBX7** | -5.72696 | 3.192329 | 2.698816 | 5.99425 | 34.8439 | 34.8556 |
| **PLK1** | -6.25246 | 6.359603 | 1.072489 | 6.489643 | 8.5339 | 5.160233 |
| **CAPRIN1** | -2.54184 | 2.730362 | 5.21687 | 2.068264 | 8.61678 | 4.309799 |
| **CDC25A** | -3.43403 | 2.409865 | -1.75409 | 0.037154 | 4.07151 | 7.003322 |
| **NUSAP1** | -3.10214 | -1.28844 | -3.84536 | -0.35916 | 3.95577 | 0.365109 |
| **HAUS4** | -5.22912 | 8.219103 | 3.310208 | 1.176557 | 3.33805 | 8.669126 |
| **SMC4** | -2.64712 | 1.701809 | -2.40529 | 1.894877 | 3.1906 | 4.003852 |
| **SPAG5** | -3.21099 | 5.599964 | 3.441051 | 3.405824 | 2.82635 | 5.186862 |
| **MYBL2** | -2.12965 | 3.382031 | 1.143602 | 3.331515 | 1.68261 | 4.827902 |
| **GTF3C4** | -6.20517 | 8.838668 | 3.631623 | 2.910432 | 0.824 | 7.267187 |
| **NIPA2** | -3.43046 | 3.864719 | 0.310266 | 2.093034 | -0.3193 | 4.631158 |
| **CDCA4** | -3.58749 | 5.027941 | 3.205815 | 1.473793 | -0.3347 | 3.40085 |
| **TCEB3** | -4.47432 | 10.15982 | 7.414412 | -0.58209 | -0.405 | 5.654366 |
| **NUP153** | -1.85129 | 1.614488 | -2.50051 | -0.23531 | -0.725 | 3.08395 |
| **WDR5** | -2.64712 | 3.503278 | -0.2338 | 0.185772 | -1.8578 | 1.130274 |
| **MCM7** | -4.80622 | 7.133993 | 1.676615 | 0.383929 | -2.5462 | 3.15251 |
| **NEK2** | -2.42586 | 4.653012 | 0.475795 | 0.780243 | -3.0597 | 2.333245 |
| **HAUS8** | -2.12787 | 3.153265 | -0.76473 | -0.82978 | -3.0676 | 1.704351 |
| **MTHFD2** | -2.93976 | 4.487436 | -0.02367 | -0.28485 | -3.168 | 0.486342 |
| **IMMT** | -3.2663 | 4.843658 | 0.504187 | -0.55732 | -3.2248 | 2.856941 |
| **C9orf40** | -4.9454 | 13.06525 | 5.267158 | 0.854552 | -3.9616 | 6.692032 |
| **HNRNPAB** | -0.12758 | -1.92381 | -5.26722 | 4.297531 | 5.17038 | 3.47 |
| **CKAP2** | -0.88594 | 0.229955 | 1.177752 | 5.957096 | 2.62599 | 1.095544 |
| **NOA1** | -0.36491 | -0.03275 | -1.03861 | 2.018725 | 1.34527 | 2.51463 |
| **MRPS9** | -0.56119 | -0.56973 | -1.49783 | 0.755474 | -0.2215 | 1.093429 |
| **CENPW** | 0.475536 | -0.49928 | -2.96797 | 3.628751 | -0.4521 | -0.14621 |
| **RMI1** | 0.213233 | 0.873644 | 1.644675 | 3.133358 | -2.1758 | -0.08923 |
| **VRK1** | 1.242818 | -0.84912 | -3.58883 | 0.35916 | 4.67724 | 2.491001 |

## SI Table 24. siRNAs.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **siRNA name** | **siRNA target** | **Accession number** | **Supplier** | **siRNA target sequence** |
| siGLO | Cyclophilin B (PPIB) | NM\_000942 | Dharmacon, UK | GAGCCCAGAUCAACCUUUA |
| CBX7 | Chromobox homolog 7 (CBX7) | NM\_175709 | Ambion, UK | GGGTAACACACACCAAGAGT |

## SI Table 25. Antibodies.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Antibody** | **Species** | **Manufacturer** | **Working dilution** | **Conditions** |
| Anti-p16 JC8 | Mouse | Prof. James Koh, Duke Cancer Institute (UK) | 1:200 | 2 hours at RT |
| Anti-p21 (12D1) | Rabbit | Cell Signalling (UK) | 1:1,000 | Overnight at 4°C |