

Supplementary Tables

A comparative study of Whi5 and retinoblastoma proteins: from sequence and structure analysis to intracellular networks

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Table S1. List of the relevant websites

| Name | URL |
|--|--|
| ANCHOR | http://anchor.enzim.hu/ |
| BioGRID | http://www.thebiogrid.org |
| BioModels | http://www.ebi.ac.uk/biomodels-main/ |
| Cell Illustrator | http://www.cellillustrator.com/ |
| CellDesigner | http://www.celldesigner.org/ |
| ClustalW2 | http://www.ebi.ac.uk/Tools/msa/clustalw2/ |
| Composition Profiler | http://www.cprofiler.org/cgi-bin/profiler.cgi/ |
| Cytoscape 2.8 | http://www.cytoscape.org/ |
| Disprot | http://www.disprot.org/ |
| | |
| FoldIndex | http://bip.weizmann.ac.il/fldbin.findex |
| Gene | http://www.ncbi.nlm.nih.gov/gene/ |
| GPS2.1 | http://gps.biocuckoo.org/ |
| iRefWeb | http://wodaklab.org/iRefWeb/ |
| NetPhosYeast | http://www.cbs.dtu.dk/services/NetPhosYeast/ |
| Pfam | http://pfam.sanger.ac.uk/ |
| PONDR®VL-XT, PONDR® VL3-BA, | http://www.pondr.com/index |
| PONDR-FIT, VSL2 | http://www.disprot.org/pondr-fit.php ; http://www.dabi.temple.edu/disprot/predictor.php |
| PPSP | http://ppsp.biocuckoo.org/index.php |
| PRALINE | http://www.ibi.vu.nl/programs/pralinewww/ |
| Proteus | http://wks80920.ccis.ualberta.ca/proteus/ |
| ProtParam | http://web.expasy.org/protparam/ |
| | |
| Revigo | http://revigo.irb.hr/ |
| rxncon | http://rxncon.org/ |
| SGD | http://www.yeastgenome.org/ |
| UniProt | http://www.uniprot.org/ |
| VSL2 | http://www.dabi.temple.edu/disprot/predictor.php |
| YPL+.db | http://yplp.uni-graz.at/index.php |

Table S2. List of the Whi5 homolog proteins analyzed in this study with BLAST search values

| Accession | Species | Length | Max identity | % Query coverage | e-value |
|----------------|--|--------|--------------|------------------|---------|
| CCF57878.1 | <i>Kazachstania africana</i> | 302 | 47% | 52 | 9e-32 |
| NP_984329.1 | <i>Ashbya gossypii</i> ATCC 10895 | 313 | 46% | 47 | 3e-27 |
| XP_002553543.1 | <i>Lachancea thermotolerans</i> CBS 6340 | 319 | 47% | 45 | 4e-27 |
| CCK72823.1 | <i>Kazachstania naganishii</i> CBS 8797 | 359 | 42% | 48 | 1e-24 |
| XP_002498613.1 | <i>Zygosaccharomyces rouxii</i> | 465 | 38% | 66% | 2e-24 |
| XP_001645731.1 | <i>Vanderwaltozyma polyspora</i> DSM 70294 | 404 | 72% | 24% | 3e-24 |
| XP_003677271.1 | <i>Naumovozyma castellii</i> CBS 4309 | 369 | 47% | 35% | 7e-24 |
| XP_003679570.1 | <i>Torulaspora delbrueckii</i> | 410 | 38% | 43% | 2e-23 |
| XP_448471.1 | <i>Candida glabrata</i> CBS 138 | 430 | 67% | 24% | 2e-22 |
| XP_003685559.1 | <i>Tetrapisispora phaffii</i> CBS 4417 | 419 | 37% | 43% | 2e-21 |
| XP_003670599.1 | <i>Naumovozyma dairenensis</i> CBS 421 | 469 | 43% | 33% | 2e-15 |
| XP_454541.1 | <i>Kluyveromyces lactis</i> NRRL Y-1140 | 370 | 32% | 44% | 1e-10 |
| CCH58702.1 | <i>Tetrapisispora blattae</i> CBS 6284 | 554 | 42% | 25% | 4e-07 |
| CCH44769.1 | <i>Wickerhamomyces ciferrii</i> | 422 | 44% | 23% | 1e-05 |

Table S3. Gravy values for sequences of full-length Whi5 and motifs 1-3. In brackets, the amino acid numbering refers to Whi5^{Sc}.

| Species | Full length | Motif 1 (136-162) | Motif 2 (173-209) | Motif 3 (245-267) |
|--------------------------|--------------------|------------------------------|------------------------------|------------------------------|
| <i>S. cerevisiae</i> | -1.153 | -0.627 | -0.689 | -0.735 |
| <i>K. africana</i> | -0.979 | -1.041 | -0.711 | -0.900 |
| <i>A. gossypii</i> | -0.712 | -0.456 | -0.605 | -0.430 |
| <i>L. thermotolerans</i> | -1.038 | -0.796 | -0.835 | -0.678 |
| <i>K. naganishii</i> | -0.842 | -0.863 | -0.632 | 0.313 |
| <i>Z. rouxii</i> | -1.163 | -0.793 | -0.546 | -0.791 |
| <i>V. polyspora</i> | -1.126 | -0.781 | -0.468 | -1.109 |
| <i>N. castellii</i> | -0.915 | -0.556 | -0.614 | -0.913 |
| <i>T. delbrueckii</i> | -0.971 | -0.667 | -0.511 | -0.983 |
| <i>C. glabrata</i> | -0.993 | -0.874 | -0.649 | -0.248 |
| <i>T. phaffii</i> | -1.075 | -0.932 | -0.746 | -0.661 |
| <i>N. dairenensis</i> | -1.138 | -0.526 | -0.581 | -0.848 |
| <i>K. lactis</i> | -0.808 | -0.689 | -0.989 | -0.595 |
| <i>T. blattae</i> | -0.868 | -0.640 | -0.522 | -0.739 |
| <i>W. ciferrii</i> | -1.260 | - | -0.597 | -0.830 |
| Average value | -1.003 | -0.732 | -0.646 | -0.708 |

Table S4. Isoelectric points of full-length sequences and motifs 1-3. In brackets, the amino acid numbering refers to Whi5^{Sc}.

| Source | Full-length | Motif 1 (136-162) | Motif 2 (173-209) | Motif 3 (245-267) |
|--------------------------|--------------------|------------------------------|------------------------------|------------------------------|
| <i>S. cerevisiae</i> | 6.28 | 10.83 | 10.23 | 6.76 |
| <i>V. polyspora</i> | 8.37 | 10.83 | 9.47 | 4.59 |
| <i>L. thermotolerans</i> | 9.48 | 10.83 | 9.16 | 4.49 |
| <i>C. glabrata</i> | 7.01 | 10.83 | 9.46 | 6.23 |
| <i>Z. rouxii</i> | 9.38 | 10.83 | 9.83 | 4.75 |
| <i>A. gossypii</i> | 6.41 | 10.83 | 8.38 | 4.91 |
| <i>K. lactis</i> | 6.33 | 5.81 | 10.12 | 6.76 |
| <i>T. phaffii</i> | 5.95 | 9.99 | 9.64 | 4.83 |
| <i>K. africana</i> | 9.20 | 10.83 | 9.46 | 8.50 |
| <i>N. castellii</i> | 5.82 | 9.99 | 9.47 | 5.07 |
| <i>T. delbrueckii</i> | 6.14 | 10.83 | 9.21 | 4.87 |
| <i>K. naganishii</i> | 8.71 | 10.84 | 8.69 | 3.43 |
| <i>N. diarenensis</i> | 9.28 | 9.01 | 6.73 | 4.65 |
| <i>T. blattae</i> | 9.56 | 11.00 | 7.10 | 4.41 |
| <i>W. ciferrii</i> | 5.38 | - | 6.03 | 4.79 |
| Average value | 7.55 | 10.23 | 8.85 | 5.26 |

Table S5. Structures of human Rb

| PDB ID | Resolution (Å) | Chain | Positions |
|---------------|-----------------------|--------------|------------------|
| 1AD6 | 2.30 | A | 378-562 |
| 1GH6 | 3.20 | B | 379-772 |
| 1GUX | 1.85 | A | 372-589 |
| | | B | 636-787 |
| 1H25 | 2.50 | E | 868-878 |
| 1N4M | 2.20 | A/B | 380-785 |
| 1O9K | 2.60 | A/C/E/G | 372-589 |
| | | B/D/F/H | 636-787 |
| 1PJM | 2.50 | A | 860-876 |
| 2AZE | 2.55 | C | 829-874 |
| 2QDJ | 2.00 | A | 52-355 |
| 2R7G | 1.67 | A/C | 380-787 |
| 3N5U | 3.20 | C | 870-882 |
| 3POM | 2.50 | A/B | 380-787 |
| 4ELJ | 2.70 | A | 53-787 |
| 4ELL | 1.98 | A/B | 380-787 |

Table S6. List of the Rb-like proteins considered in this study

| Accession | Species | Molecule | Length | Gene ID |
|----------------|--------------------------------|------------------------------|--------|-----------|
| NP_000312.2 | <i>Homo sapiens</i> | Rb 1 | 928 | 108773787 |
| NP_033055.2 | <i>Mus musculus</i> | Rb 1 | 921 | 188528630 |
| NP_989750.1 | <i>Gallus gallus</i> | Rb 1 | 921 | 45383327 |
| AAB23173.1 | <i>Xenopus laevis</i> | Rb protein | 899 | 255082 |
| NP_001071248.1 | <i>Danio rerio</i> | Rb 1 | 903 | 118150572 |
| Q24472 | <i>Drosophila melanogaster</i> | Rb family protein | 845 | - |
| Q9LKZ3 | <i>Arabidopsis thaliana</i> | Rb -related protein 1 | 1013 | - |
| Q9SLZ4 | <i>Pisum sativum</i> | Rb -related protein 1 | 1027 | - |
| NP_491686 | <i>Caenorabditis elegans</i> | Protein LIN-35 | 961 | - |
| NP_002886.2 | <i>Homo sapiens</i> | Rb -like protein 1 | 1068 | 34577079 |
| NP_035379.2 | <i>Mus musculus</i> | Rb -like protein 1 | 1063 | 213417847 |
| XP_417312.3 | <i>Gallus gallus</i> | predicted Rb -like protein 1 | 1061 | 363741428 |
| NP_001124082.1 | <i>Danio rerio</i> | Rb -like protein 1 | 1058 | 194578849 |
| NP_001084880.1 | <i>Xenopus laevis</i> | Rb-like 1 (p107) | 998 | 147905768 |
| NP_005602.3 | <i>Homo sapiens</i> | Rb -like protein 2 | 1139 | 172072597 |
| AAH20528.1 | <i>Mus musculus</i> | Rb -like 2 | 1135 | 18088202 |
| XP_002667000.2 | <i>Danio rerio</i> | predicted Rb -like protein 2 | 1087 | 326680423 |
| XP_002937369.1 | <i>Xenopus tropicalis</i> | Rb-like 2 | 1089 | 301615832 |

Table S7A. Mean distance of conserved motifs in Whi5 homologs.

Sequence of motifs were obtained by manual refinement of MEME motifs (see main text). Amino acid numbering (in brackets) refers to position in Whi5^{Sc}. Mean distances of 15 ClustalW2-aligned sequences were calculated by MEGA5.1 software with different models of amino acid substitution.

| | Mean distance calculated by | | |
|-----------------------|-----------------------------|---------------|-----------|
| | P-distance | Dayhoff model | JTT model |
| Motif 1 (136-162) | 0.326 | 0.460 | 0.459 |
| Motif 2 (173-209) | 0.298 | 0.413 | 0.427 |
| Motif 3 (250-265) | 0.346 | 0.440 | 0.468 |
| Full-length sequences | 0.522 | 0.896 | 0.927 |

Table S7B. Mean distance of sequence blocks from nine Rb orthologs.

Sequence of disordered blocks were predicted by PONDR-FIT on human Rb. Amino acid numbering (in brackets) refers to position in human Rb. Overall distances were calculated within each block of ClustalW2-aligned sequences by MEGA5 software with different models of amino acid substitution.

| | Mean distance calculated by | | |
|--------------------------|-----------------------------|---------------|-----------|
| | P-distance | Dayhoff model | JTT model |
| Disordered blocks | | | |
| I (1-56) | 0.822 | 12.335 | 5.555 |
| II (348-398) | 0.709 | 5.944 | 5.162 |
| III (605-643) | 0.686 | 2.401 | 2.100 |
| IV (858-928) | 0.707 | 3.248 | 3.451 |
| Average | 0.731 | 5.982 | 4.067 |
| Ordered blocks | | | |
| I (60-246) | 0.739 | 2.696 | 2.762 |
| II (272-338) | 0.684 | 2.586 | 2.644 |
| III (511-603) | 0.552 | 1.277 | 1.211 |
| IV (646-803) | 0.556 | 1.242 | 1.236 |
| Average | 0.633 | 1.950 | 1.963 |

Table S8. Probability scores of phosphorylation sites at the C-terminus of Rb from five vertebrate species. Probability scores were calculated by GPS2.1

| | Probability score | | | | | | | | Average probability score |
|--------------------|-------------------|------|------|------|------|------|------|-----------|---------------------------|
| <i>H. sapiens</i> | 4.90 | 5.60 | 6.70 | 5.07 | 4.15 | 5.20 | 5.21 | | 5.26 ± 0.77 |
| <i>M. musculus</i> | 4.90 | 5.60 | 5.60 | 5.00 | 4.15 | 5.20 | 5.21 | | 5.10 ± 0.50 |
| <i>G. gallus</i> | 4.90 | 5.49 | 5.62 | 5.08 | 3.79 | 4.63 | 5.22 | | 4.96 ± 0.62 |
| <i>D. rerio</i> | 5.45 | 6.11 | 5.93 | 4.77 | 5.27 | 3.92 | 5.17 | | 5.23 ± 0.74 |
| <i>X. laevis</i> | 4.94 | 5.35 | 4.60 | 5.05 | 4.89 | 5.91 | 6.06 | 3.24 4.46 | 5.26 ± 0.55 |

Table S9. Genetic/Physical interactors (G/P) of *S. cerevisiae* Whi5

| Gene Name | G/P | Protein Name | Description (from NCBI Gene database) | Function* |
|-----------|-----|---|---|---|
| ADA2 | G | Transcriptional adapter 2 | Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes | chromatin/transcription |
| AIM31 | G | Altered inheritance of mitochondria protein 31, mitochondrial | Putative protein of unknown function; GFP-fusion protein localizes to mitochondria; may interact with respiratory chain complexes III or IV; null mutant is viable and displays reduced frequency of mitochondrial genome loss | unknown |
| APA1 | G | AP4A phosphorylase | AP4A phosphorylase; bifunctional diadenosine 5',5'''-P1,P4-tetraphosphate phosphorylase and ADP sulfurylase involved in catabolism of bis(5'-nucleosidyl) tetraphosphates; catalyzes phosphorolysis of dinucleoside oligophosphates, cleaving the substrates' alpha/beta-anhydride bond and introducing Pi into the beta-position of the corresponding NDP formed; APA1 and APA2 are paralogs arising from whole genome duplication; protein abundance increases under DNA replication stress | metabolism/mitochondria |
| APL3 | G | Clathrin Adaptor Protein complex Large chain AP-2 complex subunit alpha | Alpha-adaptin, large subunit of the clathrin associated protein complex (AP-2); involved in vesicle mediated transport | cell polarity/morphogenesis |
| ASK10 | G | Activator of Skn7 | Component of RNA polymerase II holoenzyme; phosphorylated in response to oxidative stress; has a role in destruction of Ssn8p; proposed to function in activation of the glycerol channel Fps1p; ASK10 has a paralog, RGC1, that arose from the whole genome duplication | chromatin/transcription |
| ATG1 | P | Autophagy related Serine/threonine-protein kinase | Protein ser/thr kinase required for vesicle formation in autophagy and the cytoplasm-to-vacuole targeting (Cvt) pathway; structurally required for phagophore assembly site formation; during autophagy forms a complex with Atg13p and Atg17p | autophagy |
| BCK2 | G | Bypass of C Kinase | Protein rich in serine and threonine residues involved in protein kinase C signaling pathway, which controls cell integrity; overproduction suppresses pkc1 mutations | G1/S and G2/M cell cycle progression/meiosis; signaling/stress response |
| CAJ1 | G | Protein CAJ1 | Nuclear type II J heat shock protein of the E. coli dnaJ family, contains a leucine zipper-like motif, binds to non-native substrates for presentation to Ssa3p, may function during protein translocation, assembly and disassembly | unknown |
| CBC2 | G | Nuclear cap-binding protein subunit 2 | Small subunit of the heterodimeric cap binding complex that also contains Sto1p, component of the spliceosomal commitment complex; interacts with Npl3p, possibly to package mRNA for export from the nucleus; contains an RNA-binding motif | RNA processing |
| CCR4 | G | Glucose-repressible alcohol dehydrogenase | Component of the CCR4-NOT transcriptional complex, which is involved in regulation of gene expression; component of the major cytoplasmic deadenylase, which is involved in mRNA poly(A) | chromatin/transcription; RNA processing |

| | | | | |
|-------|-----|--|--|---|
| | | transcriptional effector | tail shortening | |
| CDC4 | P | E3 ubiquitin ligase complex SCF subunit CDC4 | F-box protein required for G1/S and G2/M transition, associates with Skp1p and Cdc53p to form a complex, SCFCdc4, which acts as ubiquitin-protein ligase directing ubiquitination of the phosphorylated CDK inhibitor Sic1p | protein degradation/ proteasome |
| CDC28 | G/P | Cyclin-dependent kinase 1 | Catalytic subunit of the main cell cycle cyclin-dependent kinase (CDK); alternately associates with G1 cyclins (CLNs) and G2/M cyclins (CLBs) which direct the CDK to specific substrates; involved in modulating membrane trafficking dynamics; protein abundance increases in response to DNA replication stress | G1/S and G2/M cell cycle progression/meiosis; signaling/stress response |
| CDH1 | G | CDC20 Homolog APC/C activator | Cell-cycle regulated activator of the anaphase-promoting complex/cyclosome (APC/C), which directs ubiquitination of cyclins resulting in mitotic exit; targets the APC/C to specific substrates including Cdc20p, Ase1p, Cin8p and Fin1p | protein degradation/proteasome; chromosome segregation/ kinetochore/ spindle/ microtubule |
| CKB2 | G | Casein Kinase II Beta' subunit | Beta' regulatory subunit of casein kinase 2 (CK2), a Ser/Thr protein kinase with roles in cell growth and proliferation; CK2, comprised of CKA1, CKA2, CKB1 and CKB2, has many substrates including transcription factors and all RNA polymerase | signaling/stress response |
| CLN1 | G | G1/S-specific cyclin 1 | G1 cyclin involved in regulation of the cell cycle; activates Cdc28p kinase to promote the G1 to S phase transition; late G1 specific expression depends on transcription factor complexes, MBF (Swi6p-Mbp1p) and SBF (Swi6p-Swi4p) | G1/S and G2/M cell cycle progression/meiosis; signaling/ stress response |
| CLN2 | G | G1/S-specific cyclin 2 | G1 cyclin involved in regulation of the cell cycle; activates Cdc28p kinase to promote the G1 to S phase transition; late G1 specific expression depends on transcription factor complexes, MBF (Swi6p-Mbp1p) and SBF (Swi6p-Swi4p) | G1/S and G2/M cell cycle progression/ meiosis; signaling/ stress response |
| CLN3 | G | G1/S-specific cyclin 3 | G1 cyclin involved in cell cycle progression; activates Cdc28p kinase to promote the G1 to S phase transition; plays a role in regulating transcription of the other G1 cyclins, CLN1 and CLN2; regulated by phosphorylation and proteolysis | G1/S and G2/M cell cycle progression/ meiosis; signaling/ stress response |
| COX10 | G | Protoheme IX farnesyl-transferase, mitochondrial | Heme A:farnesyltransferase, catalyzes the first step in the conversion of protoheme to the heme A prosthetic group required for cytochrome c oxidase activity; human ortholog is associated with mitochondrial disorders | metabolism/mitochondria |
| CPR7 | G | Cyclosporin-sensitive Proline Rotamase | Peptidyl-prolylcis-trans isomerase (cyclophilin), catalyzes the cis-trans isomerization of peptide bonds N-terminal to proline residues; binds to Hsp82p and contributes to chaperone activity | ER<->Golgi traffic |
| CSM3 | G | Chromosome Segregation in Meiosis protein 3 | Replication fork associated factor, required for stable replication fork pausing; component of the DNA replication checkpoint pathway; required for accurate chromosome segregation during meiosis | DNA replication/repair/HR/ cohesion |
| CTF8 | G | Chromosome Transmission Fidelity protein 8 | Subunit of a complex with Ctf18p that shares some subunits with Replication Factor C and is required for sister chromatid cohesion | DNA replication/repair/HR/ cohesion |
| DUN1 | G | DNA damage response protein kinase | Cell-cycle checkpoint serine-threonine kinase required for DNA damage-induced transcription of certain target genes, phosphorylation of Rad55p and Sml1p, and transient G2/M arrest after DNA | DNA replication/repair/HR/ cohesion |

| | | | | |
|-------|-----|--|--|---|
| | | | damage; also regulates postreplicative DNA repair | |
| EAF1 | G | ESA1p-Associated Factor | Component of the NuA4 histone acetyltransferase complex; acts as a platform for assembly of NuA4 subunits into the native complex; required for initiation of pre-meiotic DNA replication, likely due to its requirement for expression of IME1 | chromatin/transcription |
| ECM8 | G | ExtraCellular Mutant 8 | Non-essential protein of unknown function | unknown |
| ELM1 | G | Elongated Morphology 1 | Serine/threonine protein kinase that regulates cellular morphogenesis, septin behavior, and cytokinesis; required for the regulation of other kinases; forms part of the bud neck ring | cell polarity/morphogenesis; chromosome segregation/kinetochore/spindle/microtubule |
| EMI1 | G | Early Meiotic Induction protein 1 | Non-essential protein required for transcriptional induction of the early meiotic-specific transcription factor IME1, also required for sporulation; contains twin cysteine-x9-cysteine motifs | unknown |
| EMP46 | G | Protein EMP46 | Integral membrane component of endoplasmic reticulum-derived COPII-coated vesicles, which function in ER to Golgi transport | ER<->Golgi traffic |
| ENT5 | G | Epsin N-Terminal homology protein 5 | Protein containing an N-terminal epsin-like domain involved in clathrin recruitment and traffic between the Golgi and endosomes; associates with the clathrin adaptor Gga2p, clathrin adaptor complex AP-1, and clathrin | Golgi/endosome/vacuole/sorting |
| ESA1 | G/P | Histone acetyl-transferase | Catalytic subunit of the histone acetyltransferase complex (NuA4) that acetylates four conserved internal lysines of histone H4 N-terminal tail; required for cell cycle progression and transcriptional silencing at the rDNA locus | chromatin/transcription |
| FMC1 | G | ATP synthase assembly factor FMC1, mitochondrial | Mitochondrial matrix protein, required for assembly or stability at high temperature of the F1 sector of mitochondrial F1F0 ATP synthase; null mutant temperature sensitive growth on glycerol is suppressed by multicopy expression of Odc1p | drug/ion transport; metabolism/mitochondria |
| FYV7 | G | rRNA-processing protein | Essential protein required for maturation of 18S rRNA; required for survival upon exposure to K1 killer toxin | ribosome/translation |
| GPX2 | G | Glutathione Peroxidase 2 | Phospholipid hydroperoxide glutathione peroxidase; protects cells from phospholipid hydroperoxides and nonphospholipid peroxides during oxidative stress; induced by glucose starvation; protein abundance increases in response to DNA replication stress | metabolism/mitochondria |
| GSH1 | G | Glutamate-cysteine ligase | Gamma glutamylcysteine synthetase; catalyzes the first step in glutathione (GSH) biosynthesis; expression induced by oxidants, cadmium, and mercury; protein abundance increases in response to DNA replication stress | metabolism/mitochondria |
| HMT1 | G | HnRNP Methyl Transferase | Nuclear SAM-dependent mono- and asymmetric arginine dimethylating methyltransferase that modifies hnRNPs, including Npl3p and Hrp1p, affecting their activity and nuclear export; methylates U1 snRNP protein Snp1p and ribosomal protein Rps2p | ribosome/translation; nuclear-cytoplasmic transport; RNA processing |
| HOS1 | P | Histone deacetylase | Class I histone deacetylase (HDAC) family member that deacetylates Smc3p on lysine residues at anaphase onset; has sequence similarity to Hda1p, Rpd3p, Hos2p, and Hos3p; interacts with the Tup1p-Ssn6p corepressor complex | chromatin/transcription |
| HOS3 | P | Histone | Trichostatin A-insensitive homodimeric histone | chromatin/transcription |

| | | | | |
|-------|---|---|--|---|
| | | deacetylase | deacetylase (HDAC) with specificity in vitro for histones H3, H4, H2A, and H2B; similar to Hda1p, Rpd3p, Hos1p, and Hos2p; deletion results in increased histone acetylation at rDNA repeats | |
| HSL1 | G | Probable serine/threonine-protein kinase | Nim1p-related protein kinase that regulates the morphogenesis and septin checkpoints; associates with the assembled septin filament; required along with Hsl7p for bud neck recruitment, phosphorylation, and degradation of Swe1p | cell polarity/morphogenesis; G1/S and G2/M cell cycle progression/meiosis |
| HSP82 | P | ATP-dependent molecular chaperone | Hsp90 chaperone; required for pheromone signaling and negative regulation of Hsf1p; docks with Tom70p for mitochondrial preprotein delivery; promotes telomerase DNA binding and nucleotide addition; interacts with Cns1p, Cpr6p, Cpr7p, Stilp; protein abundance increases in response to DNA replication stress | signaling/stress response |
| HST3 | G | Homolog of SIR Two (SIR2) NAD-dependent histone deacetylase | Member of the Sir2 family of NAD(+)-dependent protein deacetylases; involved along with Hst4p in telomeric silencing, cell cycle progression, radiation resistance, genomic stability and short-chain fatty acid metabolism | DNA replication/repair/HR/cohesion |
| HTA1 | G | Histone H2 A | Histone H2A, core histone protein required for chromatin assembly and chromosome function; one of two nearly identical subtypes (see also HTA2); DNA damage-dependent phosphorylation by Mec1p facilitates DNA repair; acetylated by Nat4p | chromatin/transcription |
| HXT17 | G | Hexose Transporter | Hexose transporter, up-regulated in media containing raffinose and galactose at pH 7.7 versus pH 4.7, repressed by high levels of glucose | drug/ion transport; metabolism/mitochondria |
| IKI3 | G | Elongator complex protein 1 | Subunit of Elongator complex, which is required for modification of wobble nucleosides in tRNA; maintains structural integrity of Elongator; homolog of human IKAP, mutations in which cause familial dysautonomia (FD) | ribosome/translation |
| IME2 | G | Serine/threonine protein kinase (Inducer of Meiosis) | Serine/threonine protein kinase involved in activation of meiosis, associates with Ime1p and mediates its stability, activates Ndt80p; IME2 expression is positively regulated by Ime1p | G1/S and G2/M cell cycle progression/meiosis |
| ISW2 | G | ISWI chromatin-remodeling complex ATPase | ATP-dependent DNA translocase involved in chromatin remodeling; ATPase component that, with Itc1p, forms a complex required for repression of a-specific genes, INO1, and early meiotic genes during mitotic growth | chromatin/transcription |
| KEL1 | G | Kelch repeat-containing protein 1 | Protein required for proper cell fusion and cell morphology; functions in a complex with Kel2p to negatively regulate mitotic exit, interacts with Tem1p and Lte1p; localizes to regions of polarized growth; potential Cdc28p substrate | chromosome segregation/kinetochore/spindle/microtubule |
| KRE28 | G | | Subunit of a kinetochore-microtubule binding complex with Spc105p that bridges centromeric heterochromatin and kinetochore MAPs and motors, and is also required for sister chromatid bi-orientation and kinetochore binding of SAC components | chromosome segregation/kinetochore/spindle/microtubule |
| LTE1 | G | Guanine nucleotide exchange factor | Protein similar to GDP/GTP exchange factors but without detectable GEF activity; required for asymmetric localization of Bfa1p at daughter-directed spindle pole bodies and for mitotic exit at low temperatures | chromosome segregation/kinetochore/spindle/microtubule |
| MAD2 | G | Mitotic spindle checkpoint | Component of the spindle-assembly checkpoint complex; delays the onset of anaphase in cells with | chromosome segregation/kinetochore/s |

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| | | component | defects in mitotic spindle assembly; forms a complex with Mad1p; regulates APC/C activity during prometaphase and metaphase of meiosis I | pindle/microtubule |
| MBF1 | G | Multiprotein Bridging Factor 1 | Transcriptional coactivator; bridges the DNA-binding region of Gcn4p and TATA-binding protein Spt15p; suppressor of frameshift mutations; protein abundance increases in response to DNA replication stress | metabolism/ mitochondria; chromatin/transcription |
| MET12 | G | Methylene tetrahydrofolate reductase 1 | Protein with methylenetetrahydrofolate-reductase (MTHFR) activity in vitro; null mutant has no phenotype and is prototrophic for methionine; MET13 encodes major isozyme of MTHFR | metabolism/ mitochondria |
| MFB1 | G | Mitochondria-associated F-Box protein | Mitochondria-associated F-box protein involved in maintenance of normal mitochondrial morphology; interacts with Skp1p through the F-box motif; preferentially localizes to the mother cell during budding | metabolism/ mitochondria |
| MNN11 | G | Probable alpha-1,6-mannosyl transferase | Subunit of a Golgi mannosyl-transferase complex that also contains Anp1p, Mnn9p, Mnn10p, and Hoc1p, and mediates elongation of the polysaccharide mannan backbone; has homology to Mnn10p | protein folding/ protein glycosylation/ cell wall biogenesis & integrity |
| MPS3 | G | MonoPolar Spindle | Nuclear envelope protein required for SPB duplication and nuclear fusion; localizes to the SPB half bridge and at telomeres during meiosis; required with Ndj1p and Csm4p for meiotic bouquet formation and telomere-led rapid prophase movement | chromosome segregation/ kinetochore/ spindle/ microtubule |
| MSC7 | G | Putative aldehyde dehydrogenase-like protein | Protein of unknown function, green fluorescent protein (GFP)-fusion protein localizes to the endoplasmic reticulum; msc7 mutants are defective in directing meiotic recombination events to homologous chromatids | unknown |
| MSG5 | G | Tyrosine-protein phosphatase (Multicopy Suppressor of GPA1) | Dual-specificity protein phosphatase; exists in 2 isoforms; required for maintenance of a low level of signaling through the cell integrity pathway, adaptive response to pheromone; regulates and is regulated by Slr2p; dephosphorylates Fus3p | protein folding/ protein glycosylation/ cell wall biogenesis & integrity |
| MSI1 | G | Chromatin assembly factor 1 subunit p50 (Multicopy Suppressor of IRA1) | Subunit of chromatin assembly factor I (CAF-1); chromatin assembly by CAF-1 is important for multiple processes including silencing at telomeres, mating type loci, and rDNA; maintenance of kinetochore structure; deactivation of the DNA damage checkpoint after DNA repair; and chromatin dynamics during transcription; Msi1p localizes to both nucleus and cytoplasm and has an independent role as a negative regulator of the RAS/cAMP pathway via sequestration of Npr1p kinase | chromatin/transcription |
| MSN5 | P | Multicopy suppressor of SNF1 mutation | Karyopherin involved in nuclear import and export of proteins, including import of replication protein A and export of Swi6p, Far1p, and Pho4p; required for re-export of mature tRNAs after their retrograde import from the cytoplasm | G1/S and G2/M cell cycle progression/ meiosis; nuclear- cytoplasmic transport |
| NPT1 | G | Nicotinate Phosphoribosyl Transferase | Nicotinatephosphoribosyl-transferase, acts in the salvage pathway of NAD ⁺ biosynthesis; required for silencing at rDNA and telomeres and has a role in silencing at mating-type loci; localized to the nucleus | cell polarity/ morphogenesis; chromatin/ transcription |
| OM45 | G | Mitochondrial | Mitochondrial outer membrane protein of unknown | metabolism/mitochondria |

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| | | outer membrane protein | function; major constituent of the outer membrane, located on the outer (cytosolic) face; protein abundance increases in response to DNA replication stress | |
| PCI8 | G | Proteasome-COP9 signalosome (CSN)-eIF3 | Possible shared subunit of Cop9 signalosome (CSN) and eIF3, binds eIF3b subunit Prt1p, has possible dual functions in transcriptional and translational control, contains a PCI (Proteasome-COP9 signalosome (CSN)-eIF3) domain | protein degradation/proteasome |
| PCL1 | G | Pho85 Cyclin 1 | Cyclin, interacts with cyclin-dependent kinase Pho85p; member of the Pcl1,2-like subfamily, involved in the regulation of polarized growth and morphogenesis and progression through the cell cycle; localizes to sites of polarized cell growth | cell polarity/morphogenesis;G1/S and G2/M cell cycle progression/meiosis; signaling/stress response |
| PCL9 | G/P | Pho85 Cyclin 9 | Cyclin, forms a functional kinase complex with Pho85p cyclin-dependent kinase (Cdk), expressed in late M/early G1 phase, activated by Swi5p | G1/S and G2/M cell cycle progression/meiosis; signaling/stress response |
| PEP1 | G | Carboxypeptidase Y-deficient (Vacuolar protein sorting/targeting protein VPS10) | Type I transmembrane sorting receptor for multiple vacuolar hydrolases; cycles between the late-Golgi and prevacuolar endosome-like compartments | Golgi/endosome/vacuole/sorting |
| PEX30 | G | Peroxisomal membrane protein | Peroxisomal integral membrane protein, involved in negative regulation of peroxisome number; partially functionally redundant with Pex31p; genetic interactions suggest action at a step downstream of steps mediated by Pex28p and Pex29p | Unknown |
| PHO85 | G/P | Cyclin-dependent protein kinase | Cyclin-dependent kinase, with ten cyclin partners; involved in regulating the cellular response to nutrient levels and environmental conditions and progression through the cell cycle | G1/S and G2/M cell cycle progression/meiosis; chromatin/transcription |
| PKP2 | P | Pyruvate dehydrogenase kinase 2, mitochondrial | Mitochondrial protein kinase that negatively regulates activity of the pyruvate dehydrogenase complex by phosphorylating the ser-133 residue of the Pda1p subunit; acts in concert with kinase Pkp1p and phosphatases Ptc5p and Ptc6p | metabolism/mitochondria |
| PLB2 | G | Lysophospholipase 2 | Phospholipase B (lysophospholipase) involved in phospholipid metabolism; displays transacylase activity in vitro; overproduction confers resistance to lysophosphatidylcholine | lipid/sterol/fatty acid biosynthesis |
| POB3 | G | FACT complex subunit | Subunit of the heterodimeric FACT complex (Spt16p-Pob3p); FACT associates with chromatin via interaction with Nhp6Ap and Nhp6Bp, and reorganizes nucleosomes to facilitate access to DNA by RNA and DNA polymerases; protein abundance increases in response to DNA replication stress | chromatin/transcription |
| POL32 | G | DNA polymerase delta subunit 3 | Third subunit of DNA polymerase delta, involved in chromosomal DNA replication; required for error-prone DNA synthesis in the presence of DNA damage and processivity; interacts with Hys2p, PCNA (Pol30p), and Pol1p | DNA replication/repair/HR/cohesion |
| PPH21 | G | Serine/threonine-protein phosphatase PP2A-1 catalytic subunit | Catalytic subunit of protein phosphatase 2A (PP2A), functionally redundant with Pph22p; methylated at C terminus; forms alternate complexes with several regulatory subunits; involved in signal transduction and regulation of | signaling/stress response |

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| mitosis | | | | |
| PRM7 | G | Pheromone-Regulated Membrane protein | Pheromone-regulated protein, predicted to have one transmembrane segment; promoter contains Gcn4p binding elements | unknown |
| PRP4 | G | U4/U6 small nuclear ribonucleoprotein (Pre-mRNA Processing) | Splicing factor, component of the U4/U6-U5 snRNP complex | RNA processing |
| PRY1 | G | Pathogen Related in Yeast | Sterol binding protein involved in the export of acetylated sterols; secreted glycoprotein and member of the CAP protein superfamily (cysteine-rich secretory proteins (CRISP), antigen 5, and pathogenesis related 1 proteins); sterol export function is redundant with that of PRY2; may be involved in detoxification of hydrophobic compounds | unknown |
| PSR1 | G | Phosphatase | Plasma membrane associated protein phosphatase involved in the general stress response; required along with binding partner Whi2p for full activation of STRE-mediated gene expression, possibly through dephosphorylation of Msn2p | signaling/stress response |
| PTC1 | G | Phosphatase type Two C | Type 2C protein phosphatase (PP2C); dephosphorylates Hog1p, inactivating osmosensing MAPK cascade; involved in Fus3p activation during pheromone response; deletion affects precursor tRNA splicing, mitochondrial inheritance, and sporulation | signaling/stress response |
| PTK2 | P | Putative serine/threonine protein Kinase | Putative serine/threonine protein kinase involved in regulation of ion transport across plasma membrane; enhances spermine uptake | drug/ion transport; signaling/stress response |
| PTP3 | G | Protein Tyrosine Phosphatase 3 | Phosphotyrosine-specific protein phosphatase involved in the inactivation of mitogen-activated protein kinase (MAPK) during osmolarity sensing; dephosphorylates Hog1p MAPK and regulates its localization; localized to the cytoplasm | protein folding/protein glycosylation/cell wall biogenesis & integrity; cell polarity /morphogenesis;metabolism/ mitochondria; signaling/ stress response |
| PYC2 | G | Pyruvate Carboxylase 2 | Pyruvate carboxylase isoform, cytoplasmic enzyme that converts pyruvate to oxaloacetate; highly similar to isoform Pyc1p but differentially regulated; mutations in the human homolog are associated with lactic acidosis | metabolism/mitochondria |
| QCR2 | G | Ubiquinol-Cytochrome C oxidoreductase | Subunit 2 of the ubiquinol cytochrome-c reductase complex, which is a component of the mitochondrial inner membrane electron transport chain; phosphorylated; transcription is regulated by Hap1p, Hap2p/Hap3p, and heme | metabolism/mitochondria |
| RAD27 | G | Flap endonuclease 1 | 5' to 3' exonuclease, 5' flap endonuclease, required for Okazaki fragment processing and maturation as well as for long-patch base-excision repair; member of the S. pombe RAD2/FEN1 family | DNA replication/repair/HR/cohesion |
| RAD52 | G | DNA repair and recombination protein RAD52 | Protein that stimulates strand exchange by facilitating Rad51p binding to single-stranded DNA; anneals complementary single-stranded DNA; involved in the repair of double-strand breaks in DNA during vegetative growth and meiosis | DNA replication/repair/HR/cohesion |
| RAD53 | G | Serine/threonine-protein kinase | Protein kinase, required for cell-cycle arrest in response to DNA damage; activated by trans | DNA replication/repair/HR/ |

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|-------|---|---|--|---|
| | | RAD53 | autophosphorylation when interacting with hyperphosphorylated Rad9p; also interacts with ARS1 and plays a role in initiation of DNA replication | cohesion |
| RAD55 | G | DNA repair protein RAD55 | Protein that stimulates strand exchange by stabilizing the binding of Rad51p to single-stranded DNA; involved in the recombinational repair of double-strand breaks in DNA during vegetative growth and meiosis; forms heterodimer with Rad57p | DNA replication/repair/HR/cohesion |
| RAD6 | G | Radiation sensitive | Ubiquitin-conjugating enzyme (E2), involved in postreplication repair (as a heterodimer with Rad18p), DSB repair and checkpoint control (as a heterodimer with Bre1p), ubiquitin-mediated N-end rule protein degradation (as a heterodimer with Ubr1p) | chromosome segregation/kinetochore/spindle/microtubule |
| RAP1 | G | DNA-binding protein RAP1 (Repressor Activator Protein) | Essential DNA-binding transcription regulator that binds at many loci; involved in either transcription activation or repression, chromatin silencing, and telomere length maintenance; conserved protein with an N-terminal BRCT domain, a central region with homology to the Myb DNA binding domain, and a C-terminal Rap1-specific protein-interaction domain (RCT domain) | unknown |
| RGI2 | G | Respiratory growth induced | Protein of unknown function involved in energy metabolism under respiratory conditions; expression induced under carbon limitation and repressed under high glucose | unknown |
| RIM1 | G | Single-stranded DNA-binding protein RIM1, mitochondrial | Single-stranded DNA-binding protein essential for mitochondrial genome maintenance; involved in mitochondrial DNA replication | metabolism/mitochondria |
| RIM15 | G | Serine/threonine-protein kinase RIM15 | Glucose-repressible protein kinase involved in signal transduction during cell proliferation in response to nutrients, specifically the establishment of stationary phase; identified as a regulator of IME2; substrate of Pho80p-Pho85p kinase | metabolism/mitochondria;signaling/stress response |
| RKM3 | G | Ribosomal lysine (K) Methyltransferase 3 | Ribosomal lysine methyltransferase specific for monomethylation of Rpl42ap and Rpl42bp (lysine 40); nuclear SET domain containing protein | unknown |
| RLF2 | G | Rap1 protein Localization Factor | Largest subunit (p90) of the Chromatin Assembly Complex (CAF-1); chromatin assembly by CAF-1 is important for multiple processes including silencing at telomeres, mating type loci, and rDNA; maintenance of kinetochore structure; deactivation of the DNA damage checkpoint after DNA repair; and chromatin dynamics during transcription | chromatin/transcription |
| RLI1 | G | Translation initiation factor (RNase L Inhibitor) | Essential iron-sulfur protein required for ribosome biogenesis and translation initiation and termination; facilitates binding of a multifactor complex (MFC) of initiation factors to the small ribosomal subunit; predicted ABC family ATPase | ribosome/translation |
| RML2 | G | 54S ribosomal protein RML2, mitochondrial | Mitochondrial ribosomal protein of the large subunit, has similarity to E. coli L2 ribosomal protein; fat21 mutant allele causes inability to utilize oleate and may interfere with activity of the Adr1p transcription factor | metabolism/mitochondria; ribosome/translation; lipid/sterol/fatty acid biosynthesis |
| RPD3 | P | Histone deacetylase | Histone deacetylase; regulates transcription, silencing, and other processes by influencing chromatin remodeling; forms at least two different | chromatin/transcription |

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| | | | complexes which have distinct functions and members | |
| RPL14A | G | 60S ribosomal protein L14-A | Ribosomal 60S subunit protein L14A; N-terminally acetylated; homologous to mammalian ribosomal protein L14, no bacterial homolog; RPL14A has a paralog, RPL14B, that arose from the whole genome duplication | ribosome/translation |
| RPL22A | G | 60S ribosomal protein L22-A | Ribosomal 60S subunit protein L22A; required for the oxidative stress response in yeast; homologous to mammalian ribosomal protein L22, no bacterial homolog; RPL22A has a paralog, RPL22B, that arose from the whole genome duplication | ribosome/translation |
| RPL37A | G | 60S ribosomal protein L37-A | Ribosomal 60S subunit protein L37A; homologous to mammalian ribosomal protein L37, no bacterial homolog; RPL37A has a paralog, RPL37B, that arose from the whole genome duplication | ribosome/translation |
| RPS0B | G | 40S ribosomal protein S0-B | Protein component of the small (40S) ribosomal subunit; RPS0B has a paralog, RPS0A, that arose from the whole genome duplication; required for maturation of 18S rRNA along with Rps0Ap; deletion of either RPS0 gene reduces growth rate, deletion of both genes is lethal; homologous to human ribosomal protein SA and bacterial S2 | ribosome/translation |
| RRF1 | G | Ribosome Recycling Factor | Mitochondrial ribosome recycling factor, essential for mitochondrial protein synthesis and for the maintenance of the respiratory function of mitochondria | metabolism/ mitochondria; ribosome/ translation |
| RRM3 | G | ATP-dependent helicase (rDNA Recombination Mutation) | DNA helicase involved in rDNA replication and Ty1 transposition; relieves replication fork pauses at telomeric regions; structurally and functionally related to Pif1p | DNA replication/repair/HR/ cohesion |
| RSC2 | G | Chromatin structure-remodeling complex subunit | Component of the RSC chromatin remodeling complex; required for expression of mid-late sporulation-specific genes; involved in telomere maintenance | chromatin/transcription |
| RTC2 | G | Restriction of Telomere Capping | Putative vacuolar membrane transporter for cationic amino acids; likely contributes to amino acid homeostasis by exporting cationic amino acids from the vacuole; positive regulation by Lys14p suggests that lysine may be the primary substrate; member of the PQ-loop family, with seven transmembrane domains; similar to mammalian PQLC2 vacuolar transporter | unknown |
| RTS1 | G | Serine/threonine-protein phosphatase 2A 56 kDa regulatory subunit delta isoform | B-type regulatory subunit of protein phosphatase 2A (PP2A); Rts1p and Cdc55p are alternative regulatory subunits for PP2A; PP2A-Rts1p protects cohesin when recruited by Sgo1p to the pericentromere; highly enriched at centromeres in absence of Cdc55p; homolog of the mammalian B' subunit of PP2A | chromosome segregation/ kinetochore/ spindle/microtubule |
| RUD3 | G | GRIP domain-containing protein | Golgi matrix protein involved in the structural organization of the cis-Golgi; interacts genetically with COG3 and USO1 | ER<->Golgi traffic |
| SCO1 | G | Suppressor of Cytochrome Oxidase deficiency | Copper-binding protein of the mitochondrial inner membrane, required for cytochrome c oxidase activity and respiration; may function to deliver copper to cytochrome c oxidase; has similarity to thioredoxins | metabolism/mitochondria |
| SCS7 | G | Ceramide very long chain fatty acid | Sphingolipid alpha-hydroxylase, functions in the alpha-hydroxylation of sphingolipid-associated very long chain fatty acids, has both cytochrome | lipid/sterol/fatty acid biosynthesis |

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| | | hydroxylase (Suppressor of Ca ²⁺ Sensitivity) | b5-like and hydroxylase/desaturase domains, not essential for growth | |
| SHE9 | G | Sensitivity to High Expression protein 9 | Mitochondrial inner membrane protein required for normal mitochondrial morphology, may be involved in fission of the inner membrane; forms a homo-oligomeric complex | metabolism/mitochondria |
| SHR3 | G | Secretory component protein | Endoplasmic reticulum packaging chaperone, required for incorporation of amino acid permeases into COPII coated vesicles for transport to the cell surface | ER<->Golgi traffic |
| SIP4 | G | SNF1- Interacting Protein | C6 zinc cluster transcriptional activator that binds to the carbon source-responsive element (CSRE) of gluconeogenic genes; involved in the positive regulation of gluconeogenesis; regulated by Snf1p protein kinase; localized to the nucleus | metabolism/mitochondria |
| SIW14 | G | Tyrosine- protein phosphatase (Synthetic Interaction with Whi2) | Tyrosine phosphatase that plays a role in actin filament organization and endocytosis; localized to the cytoplasm | cell polarity/ morphogenesis; Golgi/endosome/vacuole/ sorting; signaling/stress response |
| SKM1 | G | STE20/PAK homologous Kinase related to Morphogenesis | Member of the PAK family of serine/threonine protein kinases with similarity to Ste20p and Cla4p; involved in down-regulation of sterol uptake; proposed to be a downstream effector of Cdc42p during polarized growth | |
| SNO1 | G | Probable glutamine amido- transferase | Protein of unconfirmed function, involved in pyridoxine metabolism; expression is induced during stationary phase; forms a putative glutamine amidotransferase complex with Snz1p, with Sno1p serving as the glutaminase | metabolism/mitochondria |
| SPS4 | G | Sporulation Specific protein 4 | Protein whose expression is induced during sporulation; not required for sporulation; heterologous expression in E. coli induces the SOS response that senses DNA damage | G1/S and G2/M cell cycle progression/ meiosis |
| SPT16 | G | FACT complex subunit | Subunit of the heterodimeric FACT complex (Spt16p-Pob3p), which associates with chromatin via interaction with Nhp6Ap and Nhp6Bp, and reorganizes nucleosomes to facilitate access to DNA by RNA and DNA polymerases | chromatin/transcription |
| SPT21 | G | Protein SPT21 | Protein with a role in transcriptional silencing; required for normal transcription at several loci including HTA2-HTB2 and HHF2-HHT2, but not required at the other histone loci; functionally related to Spt10p | chromatin/transcription |
| STB1 | G | Sin Three Binding protein | Protein with a role in regulation of MBF-specific transcription at Start, phosphorylated by Cln- Cdc28p kinases in vitro; unphosphorylated form binds Swi6p and binding is required for Stb1p function; expression is cell-cycle regulated | G1/S and G2/M cell cycle progression/ meiosis; chromatin/ transcription |
| STE50 | G | Protein STE50 | Protein involved in mating response, invasive/filamentous growth, and osmotolerance, acts as an adaptor that links G protein-associated Cdc42p-Ste20p complex to the effector Ste11p to modulate signal transduction | cell polarity/morphogenesis;si gnaling/stress response |
| SUV3 | G | ATP-dependent RNA helicase SUV3, mitochondrial | ATP-dependent RNA helicase, component of the mitochondrial degradosome along with the RNase Dss1p; the degradosome associates with the ribosome and mediates RNA turnover; also | metabolism/ mitochondria; ribosome/ translation; RNA processing |

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| | | | required during splicing of the COX1 AI5_beta intron | |
| SWD3 | G | Set1c, WD40 repeat protein | Essential subunit of the COMPASS (Set1C) complex, which methylates histone H3 on lysine 4 and is required in transcriptional silencing near telomeres; WD40 beta propeller superfamily member and ortholog of mammalian WDR5 | chromatin/transcription |
| SWI4 | P | Regulatory protein SWI4 | DNA binding component of the SBF complex (Swi4p-Swi6p), a transcriptional activator that in concert with MBF (Mbp1-Swi6p) regulates late G1-specific transcription of targets including cyclins and genes required for DNA synthesis and repair | G1/S and G2/M cell cycle progression/meiosis; chromatin/transcription |
| SWI6 | G/P | Regulatory protein SWI6 | Transcription cofactor; forms complexes with Swi4p and Mbp1p to regulate transcription at the G1/S transition; involved in meiotic gene expression; also binds Stb1p to regulate transcription at START; cell wall stress induces phosphorylation by Mpk1p, which regulates Swi6p localization; required for the unfolded protein response, independently of its known transcriptional coactivators | G1/S and G2/M cell cycle progression/meiosis; chromatin/transcription |
| TAF1 | G | TATA binding protein-Associated Factor | TFIID subunit (145 kDa), involved in RNA polymerase II transcription initiation; possesses in vitro histone acetyltransferase activity but its role in vivo appears to be minor; involved in promoter binding and G1/S progression | chromatin/transcription |
| TAF8 | G | TATA binding protein-Associated Factor | TFIID subunit (65 kDa), involved in RNA polymerase II transcription initiation | chromatin/transcription |
| TEL1 | G | Serine/threonine - protein kinase (telomere maintenance) | Protein kinase primarily involved in telomere length regulation; contributes to cell cycle checkpoint control in response to DNA damage; functionally redundant with Mec1p; regulates P-body formation induced by replication stress; homolog of human ataxia-telangiectasia mutated (ATM) gene, the gene responsible for ataxia telangiectasia (AT) (OMIM 607585) | DNA replication/repair/HR/ cohesion |
| TPK1 | P | Takashi's Protein Kinase | cAMP-dependent protein kinase catalytic subunit; promotes vegetative growth in response to nutrients via the Ras-cAMP signaling pathway; inhibited by regulatory subunit Bcy1p in the absence of cAMP; partially redundant with Tpk2p and Tpk3p | signaling/stress response |
| TPS1 | G | Trehalose-6-Phosphate Synthase | Synthase subunit of trehalose-6-P synthase/phosphatase complex; synthesizes the storage carbohydrate trehalose; also found in a monomeric form; expression is induced by the stress response and repressed by the Ras-cAMP pathway; protein abundance increases in response to DNA replication stress | metabolism/mitochondria |
| UPS3 | G | Protein UPS3, mitochondrial | Mitochondrial protein of unknown function; similar to Ups1p and Ups2p which are involved in regulation of mitochondrial cardiolipin and phosphatidylethanolamine levels; null is viable but interacts synthetically with ups1 and ups2 mutations | metabolism/mitochondria |
| VAC17 | G | Vacuole-related protein 17 | Phosphoprotein involved in vacuole inheritance; degraded in late M phase of the cell cycle; acts as a vacuole-specific receptor for myosin Myo2p | Golgi/endosome/vacuole/sorting |
| VIP1 | G | Inositol hexakisphosphat | Inositol hexakisphosphate (IP6) and inositol heptakisphosphate (IP7) kinase; IP7 production is | Golgi/endosome/vacuole/sorting |

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| | | e and diphosphoinositol-pentakisphosphate kinase | important for phosphate signaling; involved in cortical actin cytoskeleton function, and invasive pseudohyphal growth analogous to <i>S. pombe</i> asp1 | |
| VMS1 | G | VCP/Cdc48-associated Mitochondrial Stress-responsive | Component of a Cdc48p-complex involved in protein quality control; exhibits cytosolic and ER-membrane localization, with Cdc48p, during normal growth, and contributes to ER-associated degradation (ERAD) of specific substrates at a step after their ubiquitination; forms a mitochondrially-associated complex with Cdc48p and Npl4p under oxidative stress that is required for ubiquitin-mediated mitochondria-associated protein degradation (MAD); conserved in <i>C. elegans</i> and humans | unknown |
| VPS41 | G | Vacuolar protein sorting-associated protein 41 | Vacuolar membrane protein that is a subunit of the homotypic vacuole fusion and vacuole protein sorting (HOPS) complex; essential for membrane docking and fusion at the Golgi-to-endosome and endosome-to-vacuole stages of protein transport | Golgi/endosome/vacuole/sorting |
| YCK1 | P | Yeast Casein Kinase I homologue | Palmitoylated plasma membrane-bound casein kinase I isoform; shares redundant functions with Yck2p in morphogenesis, proper septin assembly, endocytic trafficking; provides an essential function overlapping with that of Yck2p | cell polarity/morphogenesis |
| YND1 | G | Yeast Nucleoside Diphosphatase | Apyrase with wide substrate specificity, helps prevent inhibition of glycosylation by hydrolyzing nucleoside tri- and diphosphates that inhibit glycotransferases; partially redundant with Gda1p; mediates adenovirus E4orf4-induced toxicity | protein folding/protein glycosylation/cell wall biogenesis&integrity |
| YPT31 | G | GTP-binding protein YPT31/YPT8 | Rab family GTPase, very similar to Ypt32p; involved in the exocytic pathway; mediates intra-Golgi traffic or the budding of post-Golgi vesicles from the trans-Golgi | cell polarity/morphogenesis |
| ZDS1 | G | Protein ZDS1 | Protein with a role in regulating Swe1p-dependent polarized growth; involved in maintaining Cdc55p in the cytoplasm where it promotes mitotic entry; involved in mitotic exit through Cdc14p regulation; interacts with silencing proteins at the telomere; has a role in Bcy1p localization; implicated in mRNA nuclear export | G1/S and G2/M cell cycle progression/meiosis; chromosome segregation/ kinetochore/spindle/ microtubule |
| ZIP1 | G | Synaptonemal complex protein ZIP1 | Transverse filament protein of the synaptonemal complex; required for normal levels of meiotic recombination and pairing between homologous chromosome during meiosis; potential Cdc28p substrate | G1/S and G2/M cell cycle progression/meiosis; chromosome segregation/ kinetochore/spindle/microtubule |
| YBR235W/VHC1 | G | Vacuolar protein Homologous to CCC family | Vacuolar membrane cation ⁺ chloride cotransporter (CCC); likely mediates K ⁺ and Cl ⁻ cotransport into the vacuole; has a role in potassium homeostasis and salt tolerance; similar to mammalian electroneutral Na ⁺ -(K ⁺)-Cl ⁻ cotransporter family | unknown |
| YGR125W | G | Uncharacterized vacuolar membrane protein | Putative protein of unknown function; deletion mutant has decreased rapamycin resistance but normal wormannin resistance; green fluorescent protein (GFP)-fusion protein localizes to the vacuole | unknown |
| YJL160C | G | Cell wall protein PIR5 | Putative protein of unknown function; member of the PIR (proteins with internal repeats) family of cell wall proteins; non-essential gene that is required for sporulation; mRNA is weakly cell | unknown |

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| | | | cycle regulated, peaking in mitosis | |
| YJR011C | G | Uncharacterized protein | Putative protein of unknown function; GFP-fusion protein expression is induced in response to the DNA-damaging agent MMS | unknown |
| YKL069W | G | Free methionine-R-sulfoxidereductase | Methionine-R-sulfoxidereductase, reduces the R enantiomer of free Met-SO, in contrast to Ycl033Cp which reduces Met-R-SO in a peptide linkage; has a role in protection against oxidative stress | nuclear-cytoplasic transport |
| YLR407W | G | Uncharacterized protein | Putative protein of unknown function; null mutant displays elongated buds and a large fraction of budded cells have only one nucleus | unknown |
| YMR160W | G | Uncharacterized protein | Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the membrane of the vacuole; mutant has enhanced sensitivity to overexpression of mutant huntingtin; YMR160W is not an essential gene | unknown |
| YMR291W/TDA1 | G | Serine/threonine-protein kinase TDA1 | Protein kinase of unknown cellular role; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and nucleus; null mutant is sensitive to expression of the top1-T722A allele; not an essential gene | unknown |
| YPL109C | G | ABC1 family protein YPL109C, mitochondrial | Putative protein of unknown function; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies | unknown |

*From Costanzo et al. 2010

Table S10A. Phosphorylation sites of *S. cerevisiae* Whi5

Listed kinases were predicted as direct physical interactors of Whi5^{Sc} (See Table 6). The phosphorylation of Whi5^{Sc} by corresponding human kinases was predicted with GPS2.1 (high threshold). The table highlights sites predicted also by NetPhosYeast server and sites experimentally confirmed.

| Yeast kinase (human homolog) | N° of sites | GPS2.1 predicted sites |
|---|--------------------|--|
| ATG1 | - | Not present in GPS2.1 |
| CDC28 (CDC2/CDK2) | 11 | <u>T5</u>, <u>T47</u>, <u>T57</u>, <u>S59</u>, <u>S62</u>, <u>T143</u>, <u>S154</u>, <u>S156</u>, <u>S161</u>, <u>T215</u>, <u>S262</u> |
| PHO85 (CDK5) | 6 | <u>T5</u>, <u>S59</u>, <u>S62</u>, <u>T143</u>, <u>S156</u>, T215 |
| PKP2 (PDK1) | 6 | T43, T181, T201, T232, <u>T275</u>, <u>T290</u> |
| PTK2 | - | Not present in GPS2.1 |
| RAD53 (RAD53/Chk2) | 5 | <u>T47</u>, <u>S78</u>, <u>S149</u>, <u>S169</u>, T170, |
| TPK1 (PKA) | 6 | T11, S12, <u>S78</u>, <u>T79</u>, S169, T170 |
| YCK1 (CK1) | 12 | S2, S9, S12, <u>S113</u>, <u>S115</u>, <u>S276</u>, <u>T281</u>, <u>T284</u>, <u>S288</u>, <u>T290</u> , T294, <u>S295</u> |
| Bold phosphorylation sites are predicted also by NetPhosYeast server Underlined phosphorylation sites are experimentally confirmed | | |

Table S10B. List of experimentally confirmed phosphorylated sites of *S. cerevisiae* Whi5 with literature references

| Residue position and type | Reference |
|--------------------------------------|--|
| T5 | (Kosugi et al., 2009;Wagner et al., 2009) |
| T47 | (de Bruin et al., 2004;Wagner et al., 2009) |
| T57 | (Holt et al., 2009;Huber et al., 2009;Wagner et al., 2009;Bodenmiller et al., 2010;Helbig et al., 2010) |
| S59 | (de Bruin et al., 2004;Smolka et al., 2007;Holt et al., 2009;Huber et al., 2009;Wagner et al., 2009;Bodenmiller et al., 2010) |
| S62 | (de Bruin et al., 2004;Gruhler et al., 2005;Smolka et al., 2007;Albuquerque et al., 2008; Gnad et al., 2009;Holt et al., 2009; Huber et al., 2009;Soufi et al., 2009; Wagner et al., 2009; Bodenmiller et al., 2010) |
| T67 | (Albuquerque et al., 2008;Bodenmiller et al., 2010) |
| S78 | (Chi et al., 2007) |
| T79 | (Chi et al., 2007;Huber et al., 2009) |

| | |
|------|--|
| T80 | (Holt et al., 2009) |
| S88 | (Holt et al., 2009;Huber et al., 2009;Wagner et al., 2009) |
| S113 | (Smolka et al., 2007;Albuquerque et al., 2008;Holt et al., 2009;Huber et al., 2009;Wagner et al., 2009;Bodenmiller et al., 2010) |
| S115 | (Smolka et al., 2007;Albuquerque et al., 2008;Holt et al., 2009;Huber et al., 2009;Wagner et al., 2009;Bodenmiller et al., 2010) |
| T143 | (Wagner et al., 2009) |
| S149 | (Wagner et al., 2009) |
| S154 | (de Bruin et al., 2004;Albuquerque et al., 2008;Holt et al., 2009;Huber et al., 2009;Wagner et al., 2009;Bodenmiller et al., 2010) |
| S156 | (de Bruin et al., 2004;Albuquerque et al., 2008;Holt et al., 2009;Huber et al., 2009;Wagner et al., 2009;Bodenmiller et al., 2010) |
| S161 | (de Bruin et al., 2004;Smolka et al., 2007;Albuquerque et al., 2008;Holt et al., 2009;Huber et al., 2009;Wagner et al., 2009;Bodenmiller et al., 2010) |
| T164 | (Huber et al., 2009;Bodenmiller et al., 2010) |
| T215 | (Wagner et al., 2009) |
| S262 | (de Bruin et al., 2004;Wagner et al., 2009) |
| S276 | (Wagner et al., 2009) |
| T281 | (Wagner et al., 2009) |
| T284 | (Holt et al., 2009) |
| S288 | (Smolka et al., 2007;Holt et al., 2009;Huber et al., 2009;Wagner et al., 2009) |
| S290 | (Holt et al., 2009;Huber et al., 2009) |

Table S10C. Phosphorylation sites of human Rb

Kinases listed were predicted as direct physical interactors of Rb. Most of them are considered in GPS2.1, used to predict specific phosphorylation sites (high threshold).

| Kinase | N° of sites | GPS2.1 predicted sites |
|--------------------------------|--------------------|---|
| ABL1 | 4 | Y498, Y606, <u>Y790</u> , <u>Y805</u> |
| AURKB | 2 | T9, <u>S360</u> |
| BRAF | | Not present in GPS2.1 |
| CDK (CDK1, CDK2, CDK4/6, CDK5) | 16 | <u>T5</u> , S179, <u>S230</u> , <u>S249</u> , <u>T252</u> , <u>T356</u> , <u>T373</u> , <u>S608</u> , <u>S612</u> , <u>S780</u> , <u>S788</u> , <u>S795</u> , <u>S807</u> , <u>S811</u> , <u>T821</u> , <u>T826</u> |
| CHEK1(CHK1) | 3 | S503, S624, T766 |
| CHEK2 | | Not present in GPS2.1 |
| DGKZ | | Not present in GPS2.1 |

| | | |
|---|----|---|
| FRK | | Not present in GPS2.1 |
| MAPK14 | 10 | <u>T5</u> , <u>T252</u> , <u>T356</u> , <u>T373</u> , <u>S612</u> , <u>S780</u> , <u>S788</u> , <u>S795</u> , <u>S811</u> , <u>T821</u> |
| MAPK9 | 7 | <u>T5</u> , <u>T252</u> , <u>S612</u> , <u>S780</u> , <u>S788</u> , <u>S811</u> , <u>T821</u> |
| PIK3R1/ PIK3R3 | | Not present in GPS2.1 |
| PRKCB | 2 | S318, S855 |
| RAF1 | 4 | T116, S350, S463, <u>S838</u> |
| Underlined phosphorylation sites are experimentally confirmed | | |

Table S10D. List of experimentally confirmed phosphorylated sites of Rb with literature references

| Residue position | Reference |
|------------------|--|
| T5 | (Lentine et al., 2012) |
| S37 | (Dephoure et al., 2008;Mayya et al., 2009;Nagano et al., 2009;Old et al., 2009;Iliuk et al., 2010;Olsen et al., 2010;Hsu et al., 2011;Shiromizu et al., 2013) |
| S230 | (Lentine et al., 2012) |
| S249 | (Brill et al., 2009;Mayya et al., 2009;Van Hoof et al., 2009;Bennetzen et al., 2010;Burke et al., 2010;Christensen et al., 2010;Olsen et al., 2010;Raijmakers et al., 2010;Hsu et al., 2011;Rigbolt et al., 2011;Lentine et al., 2012;Mitra et al., 2012;Weber et al., 2012;Shiromizu et al., 2013)(Lees et al., 1991;Rubin et al., 2001;Chytil et al., 2004;Hassler et al., 2007;Cantin et al., 2008;Dephoure et al., 2008) |
| T252 | (Lees et al., 1991;Connell-Crowley et al., 1997;Rubin et al., 2001;Chytil et al., 2004;Hassler et al., 2007;Caldon et al., 2008;Cantin et al., 2008;Dephoure et al., 2008;Mayya et al., 2009;Christensen et al., 2010;Olsen et al., 2010;Lentine et al., 2012;Mitra et al., 2012;Weber et al., 2012;Shiromizu et al., 2013) |
| Y321 | (Rikova et al., 2007;Li et al., 2009) |
| Y325 | (Rikova et al., 2007;Li et al., 2009) |
| T353 | (Wang et al., 2010) |
| T356 | (Connell-Crowley et al., 1997;Inoue et al., 2007) |
| S360 | (Chen et al., 2009) |
| T373 | (Lees et al., 1991;Connell-Crowley et al., 1997;Rubin et al., 2001;Leibundgut et al., 2005;Chen et al., 2009;Mayya et al., 2009;Old et al., 2009;Bennetzen et al., 2010;Burke et al., 2010;Iliuk et al., 2010;Wang et al., 2010;Hsu et al., 2011;Rigbolt et al., 2011;Lentine et al., 2012;Weber et al., 2012;Shiromizu et al., 2013) |
| S567 | (Ma et al., 2003;Delston et al., 2011;Mitra et al., 2012) |
| T583 | (Bennetzen et al., 2010;Rigbolt et al., 2011) |
| S608 | (Knudsen and Wang, 1997;Zarkowska and Mitnacht, 1997;Rubin et al., 2001;Burke et al., 2010;Lentine et al., 2012;Mitra et al., 2012) |
| S612 | (Knudsen and Wang, 1997;Panigone et al., 2000;Schmitz et al., 2005;Inoue et al., 2007;Burke et al., 2010;Christensen et al., 2010;Rigbolt et al., 2011;Carnevale et al., 2012;Lentine et al., 2012;Weber et al., 2012) |
| S773 | (Stokes et al., 2012) |
| T774 | (Stokes et al., 2012) |
| T778 | (Stokes et al., 2012) |

| | |
|------|--|
| S780 | (Knudsen and Wang, 1997;Panigone et al., 2000;Rubin et al., 2001;Balasenthil and Vadlamudi, 2003;Gao et al., 2003;Ma et al., 2003;Agarwal et al., 2004;Gao et al., 2004;Huang et al., 2004;Leibundgut et al., 2005;Roesch et al., 2005;Inoue et al., 2007;Sotillo et al., 2008;Burke et al., 2010;Sen et al., 2011;Lentine et al., 2012;Mitra et al., 2012;Stokes et al., 2012;Weber et al., 2012;Shiromizu et al., 2013) |
| S788 | (Connell-Crowley et al., 1997;Knudsen and Wang, 1997;Rubin et al., 2001;Rubin et al., 2005;Brill et al., 2009;Chen et al., 2009;Burke et al., 2010;Christensen et al., 2010;Rigbolt et al., 2011;Lentine et al., 2012;Stokes et al., 2012;Shiromizu et al., 2013) |
| Y790 | (Chen et al., 2009;Stokes et al., 2012) |
| S794 | (Stokes et al., 2012;Shiromizu et al., 2013) |
| S795 | (Connell-Crowley et al., 1997;Knudsen and Wang, 1997;Grafstrom et al., 1999;Panigone et al., 2000;Pan et al., 2001;Rubin et al., 2001;Simone et al., 2002;Balasenthil and Vadlamudi, 2003;Gao et al., 2003;Benzeno et al., 2004;Gao et al., 2004;Huang et al., 2004;Hamdane et al., 2005;Leibundgut et al., 2005;Roesch et al., 2005;Rubin et al., 2005;Wallick et al., 2005;Youn et al., 2005;Schmitz et al., 2006;Sundberg et al., 2006;Park et al., 2008;Chen et al., 2009;An et al., 2010;Burke et al., 2010;Boulay et al., 2011;Li et al., 2011;Lentine et al., 2012;Stokes et al., 2012;Weber et al., 2012;Shiromizu et al., 2013) |
| Y805 | (Nagano et al., 2006;Wang et al., 2010) |
| S807 | (Lees et al., 1991;Knudsen and Wang, 1996; 1997;Brantley and Harbour, 2000;Pan et al., 2001;Rubin et al., 2001;Simone et al., 2002;Balasenthil and Vadlamudi, 2003;Dimberg et al., 2003;Gao et al., 2003;Joerges et al., 2003;Ma et al., 2003;Agarwal et al., 2004;Chadee and Kyriakis, 2004;Gao et al., 2004;Ren and Rollins, 2004;de Alvaro et al., 2005;Hamdane et al., 2005;Leibundgut et al., 2005;Roesch et al., 2005;Rubin et al., 2005;Wallick et al., 2005;Youn et al., 2005;Sivaprasad et al., 2006;Sundberg et al., 2006;Sturrock et al., 2007;Dephoure et al., 2008;Park et al., 2008;Chen et al., 2009;Mayya et al., 2009;Bennetzen et al., 2010;Christensen et al., 2010;Iliuk et al., 2010;Olsen et al., 2010;Raijmakers et al., 2010;Wang et al., 2010;Clarke et al., 2011;Filippi-Chiela et al., 2011;Kennedy et al., 2011;Ku et al., 2011;Li et al., 2011;Rigbolt et al., 2011;Lentine et al., 2012;Weber et al., 2012;Shiromizu et al., 2013) |
| S811 | (Lees et al., 1991;Knudsen and Wang, 1996; 1997;Brantley and Harbour, 2000;Pan et al., 2001;Simone et al., 2002;Balasenthil and Vadlamudi, 2003;Gao et al., 2003;Joerges et al., 2003;Ma et al., 2003;Agarwal et al., 2004;Chadee and Kyriakis, 2004;Gao et al., 2004;Ren and Rollins, 2004;de Alvaro et al., 2005;Hamdane et al., 2005;Leibundgut et al., 2005;Roesch et al., 2005;Rubin et al., 2005;Wallick et al., 2005;Youn et al., 2005;Sivaprasad et al., 2006;Sundberg et al., 2006;Sturrock et al., 2007;Dephoure et al., 2008;Park et al., 2008;Chen et al., 2009;Mayya et al., 2009;Bennetzen et al., 2010;Burke et al., 2010;Christensen et al., 2010;Iliuk et al., 2010;Olsen et al., 2010;Wang et al., 2010;Clarke et al., 2011;Filippi-Chiela et al., 2011;Kennedy et al., 2011;Ku et al., 2011;Li et al., 2011;Rigbolt et al., 2011;Lentine et al., 2012;Weber et al., 2012;Shiromizu et al., 2013) |
| Y813 | (Chen et al., 2009) |
| S816 | (Bennetzen et al., 2010) |
| T821 | (Knudsen and Wang, 1996; 1997;Zarkowska and Mitnacht, 1997;Panigone et al., 2000;Rubin et al., 2001;Rubin et al., 2005;Schmitz et al., 2005;Takaki et al., 2005;Inoue et al., 2007;Wang et al., 2007;Dephoure et al., 2008;Sotillo et al., 2008;Brill et al., 2009;Chen et al., 2009;Mayya et al., 2009;Bennetzen et al., 2010;Burke et al., 2010;Olsen et al., 2010;Rigbolt et al., 2011;Sen et al., 2011;Lentine et al., 2012;Weber et al., 2012) |
| T823 | (Dephoure et al., 2008;Brill et al., 2009;Mayya et al., 2009;Bennetzen et al., 2010;Olsen et al., 2010;Rigbolt et al., 2011;Shiromizu et al., 2013) |
| T826 | (Knudsen and Wang, 1996; 1997;Zarkowska and Mitnacht, 1997;Rubin et al., 2001;Rubin et al., 2005;Takaki et al., 2005;Wang et al., 2007;Dephoure et al., 2008;Sotillo et al., 2008;Brill et al., 2009;Chen et al., 2009;Mayya et al., 2009;Sotillo et al., 2009;Bennetzen et al., 2010;Burke et al., 2010;Christensen et al., 2010;Olsen et al., 2010;Rigbolt et al., 2011;Lentine et al., 2012;Weber et al., 2012;Shiromizu et al., 2013) |
| S838 | (Mayya et al., 2009) |
| T841 | (Mayya et al., 2009) |
| S855 | (Shiromizu et al., 2013) |
| S882 | (Mayya et al., 2009) |
| S919 | (Shiromizu et al., 2013) |

Table S11. GO term enrichment of *S. cerevisiae* Whi5 interactors**Biological Process**

| GO id | GO name | adjusted-P |
|------------|---|------------|
| GO:0051726 | regulation of cell cycle | 6.51E-11 |
| GO:0006468 | protein phosphorylation | 1.72E-09 |
| GO:0051325 | interphase | 5.73E-09 |
| GO:0006464 | protein modification process | 1.60E-08 |
| GO:0007049 | cell cycle | 1.70E-08 |
| GO:0022402 | cell cycle process | 3.38E-08 |
| GO:0000082 | G1/S transition of mitotic cell cycle | 4.27E-08 |
| GO:0051329 | interphase of mitotic cell cycle | 4.61E-08 |
| GO:0048519 | negative regulation of biological process | 1.29E-07 |
| GO:0060255 | regulation of macromolecule metabolic process | 2.22E-07 |
| GO:0000083 | regulation of transcription involved in G1/S phase of mitotic cell cycle | 2.83E-07 |
| GO:0006793 | phosphorus metabolic process | 3.58E-07 |
| GO:0006796 | phosphate metabolic process | 3.58E-07 |
| GO:0022403 | cell cycle phase | 3.72E-07 |
| GO:0048523 | negative regulation of cellular process | 1.43E-06 |
| GO:0010564 | regulation of cell cycle process | 1.52E-06 |
| GO:0050789 | regulation of biological process | 2.12E-06 |
| GO:0016310 | phosphorylation | 2.78E-06 |
| GO:0043412 | macromolecule modification | 3.78E-06 |
| GO:0019222 | regulation of metabolic process | 4.16E-06 |
| GO:0050794 | regulation of cellular process | 4.50E-06 |
| GO:0065007 | biological regulation | 5.90E-06 |
| GO:0045786 | negative regulation of cell cycle | 2.15E-05 |
| GO:0080090 | regulation of primary metabolic process | 2.76E-05 |
| GO:0031323 | regulation of cellular metabolic process | 3.37E-05 |
| GO:0000278 | mitotic cell cycle | 5.28E-05 |
| GO:0007050 | cell cycle arrest | 1.60E-04 |
| GO:2000112 | regulation of cellular macromolecule biosynthetic process | 3.41E-04 |
| GO:0010556 | regulation of macromolecule biosynthetic process | 3.64E-04 |
| GO:0019219 | regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 3.81E-04 |
| GO:0051171 | regulation of nitrogen compound metabolic process | 4.22E-04 |
| GO:0006355 | regulation of transcription, DNA-dependent | 5.53E-04 |
| GO:0051276 | chromosome organization | 5.71E-04 |
| GO:0006366 | transcription from RNA polymerase II promoter | 6.60E-04 |
| GO:0000075 | cell cycle checkpoint | 6.63E-04 |
| GO:0071156 | regulation of cell cycle arrest | 6.63E-04 |
| GO:0006950 | response to stress | 7.28E-04 |
| GO:0009889 | regulation of biosynthetic process | 7.53E-04 |
| GO:0031326 | regulation of cellular biosynthetic process | 7.53E-04 |
| GO:0051252 | regulation of RNA metabolic process | 0.001056 |
| GO:0009893 | positive regulation of metabolic process | 0.001193 |
| GO:0031399 | regulation of protein modification process | 0.001249 |
| GO:0006325 | chromatin organization | 0.001321 |
| GO:0006261 | DNA-dependent DNA replication | 0.001401 |
| GO:0071900 | regulation of protein serine/threonine kinase activity | 0.001456 |
| GO:0001932 | regulation of protein phosphorylation | 0.001846 |
| GO:0010468 | regulation of gene expression | 0.002218 |
| GO:0006357 | regulation of transcription from RNA polymerase II promoter | 0.002427 |
| GO:0019220 | regulation of phosphate metabolic process | 0.002714 |
| GO:0051174 | regulation of phosphorus metabolic process | 0.002714 |

| | | |
|------------|--|----------|
| GO:0042325 | regulation of phosphorylation | 0.003345 |
| GO:0031325 | positive regulation of cellular metabolic process | 0.003669 |
| GO:0006260 | DNA replication | 0.003847 |
| GO:0048518 | positive regulation of biological process | 0.004362 |
| GO:0006351 | transcription, DNA-dependent | 0.004617 |
| GO:0032774 | RNA biosynthetic process | 0.004765 |
| GO:0007346 | regulation of mitotic cell cycle | 0.004846 |
| GO:0045859 | regulation of protein kinase activity | 0.005767 |
| GO:0033554 | cellular response to stress | 0.007291 |
| GO:0043549 | regulation of kinase activity | 0.009104 |
| GO:0006259 | DNA metabolic process | 0.009943 |
| GO:0050896 | response to stimulus | 0.01036 |
| GO:0048522 | positive regulation of cellular process | 0.010794 |
| GO:0045934 | negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 0.011587 |
| GO:0051172 | negative regulation of nitrogen compound metabolic process | 0.011587 |
| GO:0051338 | regulation of transferase activity | 0.012123 |
| GO:0043170 | macromolecule metabolic process | 0.017548 |
| GO:0051321 | meiotic cell cycle | 0.018725 |
| GO:0010605 | negative regulation of macromolecule metabolic process | 0.019471 |
| GO:0010558 | negative regulation of macromolecule biosynthetic process | 0.01977 |
| GO:2000113 | negative regulation of cellular macromolecule biosynthetic process | 0.01977 |
| GO:0044260 | cellular macromolecule metabolic process | 0.020571 |
| GO:0006348 | chromatin silencing at telomere | 0.027425 |
| GO:0010604 | positive regulation of macromolecule metabolic process | 0.031603 |
| GO:0006996 | organelle organization | 0.035544 |
| GO:0090329 | regulation of DNA-dependent DNA replication | 0.043748 |
| GO:0000279 | M phase | 0.045693 |
| GO:0009890 | negative regulation of biosynthetic process | 0.046244 |
| GO:0031327 | negative regulation of cellular biosynthetic process | 0.046244 |
| GO:0006974 | response to DNA damage stimulus | 0.052419 |
| GO:0010629 | negative regulation of gene expression | 0.058978 |
| GO:0044267 | cellular protein metabolic process | 0.063452 |
| GO:0007126 | meiosis | 0.064196 |
| GO:0051327 | M phase of meiotic cell cycle | 0.064196 |
| GO:0034401 | regulation of transcription by chromatin organization | 0.067429 |
| GO:0009892 | negative regulation of metabolic process | 0.068258 |
| GO:0006342 | chromatin silencing | 0.092364 |
| GO:0040029 | regulation of gene expression, epigenetic | 0.092364 |
| GO:0045814 | negative regulation of gene expression, epigenetic | 0.092364 |
| GO:0051716 | cellular response to stimulus | 0.093913 |
| GO:0016568 | chromatin modification | 0.119425 |
| GO:0006275 | regulation of DNA replication | 0.119668 |
| GO:0000183 | chromatin silencing at rDNA | 0.120437 |
| GO:0016458 | gene silencing | 0.122244 |
| GO:0045892 | negative regulation of transcription, DNA-dependent | 0.15543 |
| GO:0007093 | mitotic cell cycle checkpoint | 0.158093 |
| GO:0051253 | negative regulation of RNA metabolic process | 0.163068 |
| GO:0031324 | negative regulation of cellular metabolic process | 0.167291 |
| GO:0032878 | regulation of establishment or maintenance of cell polarity | 0.196574 |
| GO:0016569 | covalent chromatin modification | 0.225755 |
| GO:0016570 | histone modification | 0.225755 |
| GO:0019538 | protein metabolic process | 0.229953 |
| GO:0000086 | G2/M transition of mitotic cell cycle | 0.264798 |
| GO:0016043 | cellular component organization | 0.321617 |
| GO:2000602 | regulation of interphase of mitotic cell cycle | 0.361641 |
| GO:0090304 | nucleic acid metabolic process | 0.36275 |
| GO:0031331 | positive regulation of cellular catabolic process | 0.374178 |
| GO:0048478 | replication fork protection | 0.382576 |

| | | |
|------------|--|----------|
| GO:0045935 | positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 0.409212 |
| GO:0051173 | positive regulation of nitrogen compound metabolic process | 0.427331 |
| GO:0071824 | protein-DNA complex subunit organization | 0.439733 |
| GO:0009891 | positive regulation of biosynthetic process | 0.499493 |
| GO:0031328 | positive regulation of cellular biosynthetic process | 0.499493 |
| GO:0065004 | protein-DNA complex assembly | 0.512427 |
| GO:0000079 | regulation of cyclin-dependent protein kinase activity | 0.523402 |
| GO:0071842 | cellular component organization at cellular level | 0.558951 |
| GO:0010948 | negative regulation of cell cycle process | 0.582085 |
| GO:0051301 | cell division | 0.65614 |
| GO:0009987 | cellular process | 0.74241 |
| GO:0051052 | regulation of DNA metabolic process | 0.781592 |
| GO:0006281 | DNA repair | 0.792892 |
| GO:0090068 | positive regulation of cell cycle process | 0.829798 |
| GO:0070933 | histone H4 deacetylation | 0.88995 |
| GO:0071511 | inactivation of MAPK activity involved in conjugation with cellular fusion | 0.88995 |
| GO:0016311 | dephosphorylation | 0.91968 |
| GO:0065009 | regulation of molecular function | 0.968874 |
| GO:0051254 | positive regulation of RNA metabolic process | 0.98764 |

Cellular Component

| GO id | GO name | adjusted-P |
|------------|--|------------|
| GO:0005634 | nucleus | 0.008155 |
| GO:0000307 | cyclin-dependent protein kinase holoenzyme complex | 0.049758 |
| GO:0033309 | SBF transcription complex | 0.080839 |
| GO:0043234 | protein complex | 0.08831 |
| GO:0005694 | chromosome | 0.105131 |
| GO:0043226 | organelle | 0.113141 |
| GO:0043229 | intracellular organelle | 0.113141 |
| GO:0044427 | chromosomal part | 0.198173 |
| GO:0043227 | membrane-bounded organelle | 0.204465 |
| GO:0043231 | intracellular membrane-bounded organelle | 0.204465 |
| GO:0044424 | intracellular part | 0.406627 |
| GO:0044454 | nuclear chromosome part | 0.445641 |
| GO:0000228 | nuclear chromosome | 0.519499 |
| GO:0005622 | intracellular | 0.557018 |
| GO:0035101 | FACT complex | 0.88995 |

Molecular Function

| GO id | GO name | adjusted-P |
|------------|---|------------|
| GO:0004672 | protein kinase activity | 8.61E-05 |
| GO:0004674 | protein serine/threonine kinase activity | 3.01E-04 |
| GO:0016773 | phosphotransferase activity, alcohol group as acceptor | 0.012721 |
| GO:0016301 | kinase activity | 0.014484 |
| GO:0019887 | protein kinase regulator activity | 0.119668 |
| GO:0019207 | kinase regulator activity | 0.158093 |
| GO:0034739 | histone deacetylase activity (H3-K16 specific) | 0.196574 |
| GO:0004721 | phosphoprotein phosphatase activity | 0.29924 |
| GO:0016772 | transferase activity, transferring phosphorus-containing groups | 0.373824 |
| GO:0031078 | histone deacetylase activity (H3-K14 specific) | 0.382576 |
| GO:0032041 | NAD-dependent histone deacetylase activity (H3-K14 specific) | 0.382576 |
| GO:0032129 | histone deacetylase activity (H3-K9 specific) | 0.382576 |
| GO:0046969 | NAD-dependent histone deacetylase activity (H3-K9 specific) | 0.382576 |

| | | |
|------------|--|----------|
| GO:0046970 | NAD-dependent histone deacetylase activity (H4-K16 specific) | 0.382576 |
| GO:0016538 | cyclin-dependent protein kinase regulator activity | 0.436498 |
| GO:0004407 | histone deacetylase activity | 0.497424 |
| GO:0033558 | protein deacetylase activity | 0.497424 |
| GO:0005524 | ATP binding | 0.554189 |
| GO:0032559 | adenylnucleotide binding | 0.582085 |
| GO:0030554 | adenyl nucleotide binding | 0.643843 |

Table S12. Interactors of human Rb protein

| Gene Name | Protein Name | Description (from NCBI Gene database) | Function |
|-----------|--|--|--|
| AATF | apoptosis antagonizing transcription factor | It contains a leucine zipper, which is a characteristic motif of transcription factors, and was shown to exhibit strong transactivation activity when fused to Gal4 DNA binding domain. Overexpression of this gene interfered with MAP3K12 induced apoptosis. | Apoptosis |
| ABL1 | c-abl oncogene 1, non-receptor tyrosine kinase | The ABL1 protooncogene encodes a cytoplasmic and nuclear protein tyrosine kinase that has been implicated in processes of cell differentiation, cell division, cell adhesion, and stress response. Activity of c-Abl protein is negatively regulated by its SH3 domain, and deletion of the SH3 domain turns ABL1 into an oncogene. The t(9;22) translocation results in the head-to-tail fusion of the BCR (MIM:151410) and ABL1 genes present in many cases of chronic myelogenous leukemia. The DNA-binding activity of the ubiquitously expressed ABL1 tyrosine kinase is regulated by CDC2-mediated phosphorylation, suggesting a cell cycle function for ABL1. | Signaling/stress response |
| AHR | aryl hydrocarbon receptor | It is a ligand-activated transcription factor involved in the regulation of biological responses to planar aromatic hydrocarbons. This receptor has been shown to regulate xenobiotic-metabolizing enzymes such as cytochrome P450. Its ligands included a variety of aromatic hydrocarbons. | Apoptosis |
| ANAPC2 | anaphase promoting complex subunit 2 | A large protein complex, termed the anaphase-promoting complex (APC), or the cyclosome, promotes metaphase-anaphase transition by ubiquitinating its specific substrates such as mitotic cyclins and anaphase inhibitor, which are subsequently degraded by the 26S proteasome. | Apoptosis |
| AR | androgen receptor | The androgen receptor gene is more than 90 kb long and codes for a protein that has 3 major functional domains: the N-terminal domain, DNA-binding domain, and androgen-binding domain. The protein functions as a steroid-hormone activated transcription factor. Upon binding the hormone ligand, the receptor dissociates from accessory proteins, translocates into the nucleus, dimerizes, and then stimulates transcription of androgen responsive genes. | G1/S and G2/M cell cycle progression/meiosis |
| ARID3B | AT rich interactive domain 3B (BRIGHT-like) | It is a member of the ARID (AT-rich interaction domain) family of DNA-binding proteins. Members of the ARID family have roles in embryonic patterning, cell lineage gene regulation, cell cycle control, transcriptional regulation and possibly in chromatin structure modification. | Chromatin/transcription |
| ARID4A | AT rich interactive domain 4A (RBP1-like) | It binds directly, with several other proteins, to retinoblastoma protein (pRB). This protein, in turn, serves as a bridging molecule to recruit HDACs and, in addition, provides a second HDAC-independent repression function. The protein possesses transcriptional repression activity. | Chromatin/transcription |
| ARNT | aryl hydrocarbon receptor nuclear translocator | The aryl hydrocarbon (Ah) receptor is involved in the induction of several enzymes that participate in xenobiotic metabolism. The ligand-free, cytosolic form of the Ah receptor is complexed to heat shock protein 90. Binding of ligand, which includes dioxin and polycyclic aromatic hydrocarbons, results in translocation of the ligand-binding subunit only to the nucleus. Induction of enzymes involved in xenobiotic metabolism occurs through binding of the ligand-bound Ah receptor to xenobiotic responsive elements in the promoters of genes for these enzymes. | Chromatin/transcription |
| ATF2 | activating transcription factor 2 | It is a member of the leucine zipper family of DNA binding proteins. This protein binds to the cAMP-responsive element (CRE), an octameric palindrome. It forms a homodimer or a heterodimer with c-Jun and stimulates CRE-dependent transcription. This protein is also a histone acetyltransferase (HAT) that specifically acetylates histones H2B and H4 in vitro. | Chromatin/transcription |

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| AURKB | aurora kinase B | It is a member of the aurora kinase subfamily of serine/threonine kinases. These kinases participate in the regulation of segregation of chromosomes during mitosis and meiosis through association with microtubules. | chromosome segregation/ kinetochore/ spindle/ microtubule |
| BAG1 | BCL2-associated athanogene | The oncogene BCL2 is a membrane protein that blocks a step in a pathway leading to apoptosis or programmed cell death. The protein binds to BCL2 and is referred to as BCL2-associated athanogene. It enhances the anti-apoptotic effects of BCL2 and represents a link between growth factor receptors and anti-apoptotic mechanisms. | Apoptosis |
| BCR | breakpoint cluster region | It is involved in Philadelphia chromosome. Although the BCR-ABL fusion protein has been extensively studied, the function of the normal BCR gene product is not clear. The protein has serine/threonine kinase activity and is a GTPase-activating protein for p21rac. | Unknown |
| BRCA1 | breast cancer 1, early onset | It is a nuclear phosphoprotein that plays a role in maintaining genomic stability, and it also acts as a tumor suppressor. The protein combines with other tumor suppressors, DNA damage sensors, and signal transducers to form a large multi-subunit protein complex known as the BRCA1-associated genome surveillance complex (BASC). This protein associates with RNA polymerase II, and through the C-terminal domain, also interacts with histone deacetylase complexes. This protein thus plays a role in transcription, DNA repair of double-stranded breaks, and recombination. | DNA replication/ repair/HR/ cohesion |
| BRF1 | BRF1 homolog, subunit of RNA polymerase III transcription initiation factor IIIB (S. cerevisiae) | It is one of the three subunits of the RNA polymerase III transcription factor complex. This complex plays a central role in transcription initiation by RNA polymerase III on genes encoding tRNA, 5S rRNA, and other small structural RNAs. The gene product belongs to the TF2B family. | Chromatin/ transcription |
| CBX1 | chromobox homolog 1 | It is a highly conserved nonhistone protein, which is a member of the heterochromatin protein family. The protein is enriched in the heterochromatin and associated with centromeres. The protein has a single N-terminal chromodomain, which can bind to histone proteins via methylated lysine residues, and a C-terminal chromo shadow-domain (CSD) which is responsible for the homodimerization and interaction with a number of chromatin-associated nonhistone proteins. | Chromatin/ transcription |
| CBX4 | chromobox homolog 4 | Same as CBX1 | Chromatin/ transcription |
| CBX5 | chromobox homolog 5 | Same as CBX1 | Chromatin/ transcription |
| CCNA1 | cyclin A1 | The cyclin encoded by this gene was shown to be expressed in testis and brain, as well as in several leukemic cell lines, and is thought to primarily function in the control of the germline meiotic cell cycle. This cyclin binds both CDK2 and CDC2 kinases, which give two distinct kinase activities, one appearing in S phase, the other in G2, and thus regulate separate functions in cell cycle. This cyclin was found to bind to important cell cycle regulators, such as Rb family proteins, transcription factor E2F-1, and the p21 family proteins. | G1/S and G2/M cell cycle progression/ meiosis |
| CCNA2 | cyclin A2 | In contrast to cyclin A1, which is present only in germ cells, this cyclin is expressed in all tissues tested. This cyclin binds and activates CDC2 or CDK2 kinases, and thus promotes both cell cycle G1/S and G2/M transitions. | G1/S and G2/M cell cycle progression/ meiosis |
| CCND1 | cyclin D1 | This cyclin forms a complex with and functions as a regulatory subunit of CDK4 or CDK6, whose activity is required for cell cycle G1/S transition. This protein has been shown to interact with tumor suppressor protein Rb and the expression of this gene is regulated positively by Rb. | G1/S and G2/M cell cycle progression/ meiosis |
| CCND2 | cyclin D2 | Same as CCND1. Knockout studies of the homologous gene in mouse suggest the essential roles of this gene in ovarian granulosa and germ | G1/S and G2/M cell cycle |

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| | | cell proliferation. High-level expression of this gene was observed in ovarian and testicular tumors. | progression/ meiosis |
| CCND3 | cyclin D3 | Same as CCND1. The CDK4 activity associated with this cyclin was reported to be necessary for cell cycle progression through G2 phase into mitosis after UV radiation. Several transcript variants encoding different isoforms have been found for this gene. | G1/S and G2/M cell cycle progression/ meiosis |
| CCNE1 | cyclin E1 | This cyclin forms a complex with and functions as a regulatory subunit of CDK2, whose activity is required for cell cycle G1/S transition. This protein accumulates at the G1-S phase boundary and is degraded as cells progress through S phase. Overexpression of this gene has been observed in many tumors, which results in chromosome instability, and thus may contribute to tumorigenesis. This protein was found to associate with, and be involved in, the phosphorylation of NPAT protein (nuclear protein mapped to the ATM locus), which participates in cell-cycle regulated histone gene expression and plays a critical role in promoting cell-cycle progression in the absence of pRb. | G1/S and G2/M cell cycle progression/ meiosis |
| CCNT2 | cyclin T2 | This cyclin and its kinase partner CDK9 were found to be subunits of the transcription elongation factor p-TEFb. The p-TEFb complex containing this cyclin was reported to interact with, and act as a negative regulator of human immunodeficiency virus type 1 (HIV-1) Tat protein. | Chromatin/ transcription |
| CDC16 | cell division cycle 16 homolog (S. cerevisiae) | It is a component protein of the APC complex, which is composed of eight proteins and functions as a protein ubiquitin ligase. This protein and two other APC complex proteins, CDC23 and CDC27, contain a tetratricopeptide repeat (TPR), a protein domain that may be involved in protein-protein interaction. | protein degradation/ proteosome |
| CDC27 | cell division cycle 27 homolog (S. cerevisiae) | This protein is a component of anaphase-promoting complex (APC), which is composed of eight protein subunits and highly conserved in eucaryotic cells. APC catalyzes the formation of cyclin B-ubiquitin conjugate that is responsible for the ubiquitin-mediated proteolysis of B-type cyclins. This protein and 3 other members of the APC complex contain the TPR (tetratricopeptide repeat), a protein domain important for protein-protein interaction. This protein was shown to interact with mitotic checkpoint proteins including Mad2, p55CDC and BUBR1, and thus may be involved in controlling the timing of mitosis. | protein degradation/ proteosome |
| CDK1 | cyclin- dependent kinase 1 | This protein is a catalytic subunit of the highly conserved protein kinase complex known as M-phase promoting factor (MPF), which is essential for G1/S and G2/M phase transitions of eukaryotic cell cycle. Mitotic cyclins stably associate with this protein and function as regulatory subunits. The kinase activity of this protein is controlled by cyclin accumulation and destruction through the cell cycle. The phosphorylation and dephosphorylation of this protein also play important regulatory roles in cell cycle control. | G1/S and G2/M cell cycle progression/ meiosis |
| CDK2 | cyclin- dependent kinase 2 | This protein kinase is highly similar to the gene products of <i>S. cerevisiae</i> cdc28, and <i>S. pombe</i> cdc2. It is a catalytic subunit of the cyclin-dependent protein kinase complex, whose activity is restricted to the G1-S phase, and essential for cell cycle G1/S phase transition. This protein associates with and regulated by the regulatory subunits of the complex including cyclin A or E, CDK inhibitor p21Cip1 (CDKN1A) and p27Kip1 (CDKN1B). Its activity is also regulated by its protein phosphorylation. | G1/S and G2/M cell cycle progression/ meiosis |
| CDK4 | cyclin- dependent kinase 4 | This protein is highly similar to the gene products of <i>S. cerevisiae</i> cdc28 and <i>S. pombe</i> cdc2. It is a catalytic subunit of the protein kinase complex that is important for cell cycle G1 phase progression. The activity of this kinase is restricted to the G1-S phase, which is controlled by the regulatory subunits D-type cyclins and CDK inhibitor p16(INK4a). This kinase was shown to be responsible for the phosphorylation pRb. Mutations in this gene as well as in its related proteins including D-type cyclins, p16(INK4a) and Rb were all found to be associated with tumorigenesis of a variety of cancers. | G1/S and G2/M cell cycle progression/ meiosis |
| CDK5 | cyclin- dependent | Proline-directed serine/threonine-protein kinase essential for neuronal cell cycle arrest and differentiation and may be involved in apoptotic cell | Cell Differentiation |

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| | kinase 5 | death in neuronal diseases by triggering abortive cell cycle re-entry. Interacts with D1 and D3-type G1 cyclins. | |
| CDK6 | cyclin-dependent kinase 6 | This kinase is a catalytic subunit of the protein kinase complex that is important for cell cycle G1 phase progression and G1/S transition. The activity of this kinase first appears in mid-G1 phase, which is controlled by the regulatory subunits including D-type cyclins and members of INK4 family of CDK inhibitors. This kinase, as well as CDK4, has been shown to phosphorylate, and thus regulate the activity of, tumor suppressor protein Rb. Expression of this gene is up-regulated in some types of cancer. | G1/S and G2/M cell cycle progression/meiosis |
| CDK9 | cyclin-dependent kinase 9 | This kinase was found to be a component of the multiprotein complex TAK/P-TEFb, which is an elongation factor for RNA polymerase II-directed transcription and functions by phosphorylating the C-terminal domain of the largest subunit of RNA polymerase II. This protein forms a complex with and is regulated by its regulatory subunit cyclin T or cyclin K. HIV-1 Tat protein was found to interact with this protein and cyclin T, which suggested a possible involvement of this protein in AIDS. | Chromatin/transcription |
| CEBPA | CCAAT/enhancer binding protein (C/EBP), alpha | The protein encoded by this intronless gene is a bZIP transcription factor that can bind as a homodimer to certain promoters and enhancers. It can also form heterodimers with the related proteins CEBP-beta and CEBP-gamma. The protein has been shown to bind to the promoter and modulate the expression of the gene encoding leptin, a protein that plays an important role in body weight homeostasis. Also, the protein can interact with CDK2 and CDK4, thereby inhibiting these kinases and causing growth arrest in cultured cells. | Immune Response |
| CEBPB | CCAAT/enhancer binding protein (C/EBP), beta | The encoded protein is important in the regulation of genes involved in immune and inflammatory responses and has been shown to bind to the IL-1 response element in the IL-6 gene, as well as to regulatory regions of several acute-phase and cytokine genes. In addition, the encoded protein can bind the promoter and upstream element and stimulate the expression of the collagen type I gene. | Immune Response |
| CREG1 | cellular repressor of E1A-stimulated genes 1 | The adenovirus E1A protein both activates and represses gene expression to promote cellular proliferation and inhibit differentiation. The protein encoded by this gene antagonizes transcriptional activation and cellular transformation by E1A. This protein shares limited sequence similarity with E1A and binds both the general transcription factor TBP and the tumor suppressor pRb in vitro. | Cell Differentiation |
| CUX1 | cut-like homeobox 1 | The protein encoded by this gene is a member of the homeodomain family of DNA binding proteins. It may regulate gene expression, morphogenesis, and differentiation and it may also play a role in the cell cycle progression. | Immune Response |
| DNAJA2 | DnaJ (Hsp40) homolog, subfamily A, member 2 | The protein encoded by this gene belongs to the evolutionarily conserved DNAJ/HSP40 family of proteins, which regulate molecular chaperone activity by stimulating ATPase activity. DNAJ proteins may have up to 3 distinct domains: a conserved 70-amino acid J domain, usually at the N terminus; a glycine/phenylalanine (G/F)-rich region; and a cysteine-rich domain containing 4 motifs resembling a zinc finger domain. The product of this gene works as a cochaperone of Hsp70s in protein folding and mitochondrial protein import in vitro. | protein folding/protein glycosylation/cell wall biogenesis& integrity |
| DNMT1 | DNA (cytosine-5-)-methyltransferase 1 | DNA (cytosine-5-)-methyltransferase 1 has a role in the establishment and regulation of tissue-specific patterns of methylated cytosine residues. Aberrant methylation patterns are associated with certain human tumors and developmental abnormalities. | Chromatin/transcription |
| DNMT3A | DNA (cytosine-5-)-methyltransferase 3 alpha | It is a DNA methyltransferase that is thought to function in de novo methylation, rather than maintenance methylation. The protein localizes to the cytoplasm and nucleus and its expression is developmentally regulated. | Chromatin/transcription |
| E2F1 | E2F transcription factor 1 | The E2F family plays a crucial role in the control of cell cycle and action of tumor suppressor proteins and is also a target of the transforming proteins of small DNA tumor viruses. The E2F proteins contain several | G1/S and G2/M cell cycle progression/ |

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| | | evolutionally conserved domains found in most members of the family. These domains include a DNA binding domain, a dimerization domain that determines interaction with the differentiation regulated transcription factor proteins (DP), a transactivation domain enriched in acidic amino acids, and a tumor suppressor protein association domain which is embedded within the transactivation domain. This protein binds preferentially to retinoblastoma protein pRB in a cell-cycle dependent manner. It can mediate both cell proliferation and p53-dependent/independent apoptosis. | meiosis |
| E2F2 | E2F transcription factor 2 | Same as E2F1. This protein binds specifically to retinoblastoma protein pRB in a cell-cycle dependent manner, and it exhibits overall 46% amino acid identity to E2F1. | G1/S and G2/M cell cycle progression/meiosis |
| E2F4 | E2F transcription factor 4, p107/p130-binding | Same as E2F1. This protein binds to all three of the tumor suppressor proteins pRB, p107 and p130, but with higher affinity to the last two. It plays an important role in the suppression of proliferation-associated genes, and its gene mutation and increased expression may be associated with human cancer. | G1/S and G2/M cell cycle progression/meiosis |
| E4F1 | E4F transcription factor 1 | The zinc finger protein encoded by this gene is one of several cellular transcription factors whose DNA-binding activities are regulated through the action of adenovirus E1A. A 50-kDa amino-terminal product is generated from the full-length protein through proteolytic cleavage. The protein is differentially regulated by E1A-induced phosphorylation. The full-length gene product represses transcription from the E4 promoter in the absence of E1A, while the 50-kDa form acts as a transcriptional activator in its presence. | G1/S and G2/M cell cycle progression/meiosis |
| EID1 | EP300 interacting inhibitor of differentiation 1 | Interacts with pRb and EP300 and acts as a repressor of MYOD1 transactivation. Inhibits EP300 and CBP histone acetyltransferase activity. May be involved in coupling cell cycle exit to the transcriptional activation of genes required for cellular differentiation. May act as a candidate coinhibitory factor for NR0B2 that can be directly linked to transcription inhibitory mechanisms. | Cell Differentiation |
| ENC1 | ectodermal-neural cortex 1 (with BTB-like domain) | It is a member of the kelch-related family of actin-binding proteins. The encoded protein plays a role in the oxidative stress response as a regulator of the transcription factor Nrf2, and expression of this gene may play a role in malignant transformation. | Cell Differentiation |
| FOXM1 | forkhead box M1 | The protein encoded by this gene is a transcriptional activator involved in cell proliferation. The encoded protein is phosphorylated in M phase and regulates the expression of several cell cycle genes, such as cyclin B1 and cyclin D1. Several transcript variants encoding different isoforms have been found for this gene. | G1/S and G2/M cell cycle progression/meiosis |
| FRK | fyn-related kinase | The protein encoded by this gene belongs to the TYR family of protein kinases. This tyrosine kinase is a nuclear protein and may function during G1 and S phase of the cell cycle and suppress growth. | G1/S and G2/M cell cycle progression/meiosis |
| FZR1 | fizzy/cell division cycle 20 related 1 (Drosophila) | Key regulator of ligase activity of the anaphase promoting complex/cyclosome (APC/C), which confers substrate specificity upon the complex. Associates with the APC/C in late mitosis, in replacement of CDC20, and activates the APC/C during anaphase and telophase. At the G1/S transition FZR1 is phosphorylated, leading to its dissociation from the APC/C. Following DNA damage, it is required for the G2 DNA damage checkpoint: its dephosphorylation and reassociation with the APC/C leads to the ubiquitination of PLK1, preventing entry into mitosis. | protein degradation/proteasome |
| GNB2L1 | guanine nucleotide binding protein (G protein), beta polypeptide 2-like 1 | Involved in the recruitment, assembly and/or regulation of a variety of signaling molecules. Interacts with a wide variety of proteins and plays a role in many cellular processes. Component of the 40S ribosomal subunit involved in translational repression. Binds to and stabilizes activated protein kinase C (PKC), increasing PKC-mediated phosphorylation. May recruit activated PKC to the ribosome, leading to phosphorylation of EIF6. | Unknown |

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| GTF3C1 | general transcription factor IIIC, polypeptide 1, alpha 220kDa | Required for RNA polymerase III-mediated transcription. Component of TFIIC that initiates transcription complex assembly on tRNA and is required for transcription of 5S rRNA and other stable nuclear and cytoplasmic RNAs. Binds to the box B promoter element. | Chromatin/transcription |
| HBP1 | HMG-box transcription factor 1 | Transcriptional repressor that binds to the promoter region of target genes. Plays a role in the regulation of the cell cycle and of the Wnt pathway. Binds preferentially to the sequence 5'-TTCATTTCATTCA-3'. Binding to the H1F0 promoter is enhanced by interaction with RB1. Disrupts the interaction between DNA and TCF4. | G1/S and G2/M cell cycle progression/meiosis |
| HDAC1 | histone deacetylase 1 | The protein belongs to the histone deacetylase/acuc/apha family and is a component of the histone deacetylase complex. It also interacts with retinoblastoma tumor-suppressor protein and this complex is a key element in the control of cell proliferation and differentiation. Together with metastasis-associated protein-2, it deacetylates p53 and modulates its effect on cell growth and apoptosis. | Chromatin/transcription |
| HDAC2 | histone deacetylase 2 | The protein belongs to the histone deacetylase family. Histone deacetylases act via the formation of large multiprotein complexes, and are responsible for the deacetylation of lysine residues at the N-terminal regions of core histones (H2A, H2B, H3 and H4). This protein forms transcriptional repressor complexes by associating with many different proteins, including YY1, a mammalian zinc-finger transcription factor. Thus, it plays an important role in transcriptional regulation, cell cycle progression and developmental events. | Chromatin/transcription |
| HDAC3 | histone deacetylase 3 | The protein belongs to the histone deacetylase/acuc/apha family. It has histone deacetylase activity and represses transcription when tethered to a promoter. It may participate in the regulation of transcription through its binding with the zinc-finger transcription factor YY1. This protein can also down-regulate p53 function and thus modulate cell growth and apoptosis. | Chromatin/transcription |
| HMGA2 | high mobility group AT-hook 2 | It is a protein belonging to the non-histone chromosomal high mobility group (HMG) protein family. HMG proteins function as architectural factors and are essential components of the enhancosome. This protein contains structural DNA-binding domains and may act as a transcriptional regulating factor. Identification of the deletion, amplification, and rearrangement of this gene that are associated with myxoid liposarcoma suggests a role in adipogenesis and mesenchymal differentiation. A gene knock out study of the mouse counterpart demonstrated that this gene is involved in diet-induced obesity. | Chromatin/transcription |
| HMGB1 | high mobility group box 1 | DNA binding proteins that associates with chromatin and has the ability to bend DNA. Binds preferentially single-stranded DNA. Involved in V(D)J recombination by acting as a cofactor of the RAG complex. Acts by stimulating cleavage and RAG protein binding at the 23 bp spacer of conserved recombination signal sequences (RSS). | DNA replication/repair/HR/cohesion |
| IRF3 | interferon regulatory factor 3 | It is a member of the interferon regulatory transcription factor (IRF) family. The encoded protein is found in an inactive cytoplasmic form that upon serine/threonine phosphorylation forms a complex with CREBBP. This complex translocates to the nucleus and activates the transcription of interferons alpha and beta, as well as other interferon-induced genes. | signaling/stress response |
| JUN | jun proto-oncogene | The protein which is highly similar to the viral protein, and which interacts directly with specific target DNA sequences to regulate gene expression. This gene is intronless and is mapped to 1p32-p31, a chromosomal region involved in both translocations and deletions in human malignancies. | Chromatin/transcription |
| KAT2B | K(lysine) acetyltransferase 2B | CBP and p300 are large nuclear proteins that bind to many sequence-specific factors involved in cell growth and/or differentiation, including c-jun and the adenoviral oncoprotein E1A. The protein encoded by this gene associates with p300/CBP. It has in vitro and in vivo binding activity with CBP and p300, and competes with E1A for binding sites in p300/CBP. It has histone acetyl transferase activity with core histones | Chromatin/transcription |

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| | | and nucleosome core particles, indicating that this protein plays a direct role in transcriptional regulation. | |
| KAT5 | K(lysine) acetyltransferase 5 | The protein belongs to the MYST family of histone acetyl transferases (HATs) and was originally isolated as an HIV-1 TAT-interactive protein. HATs play important roles in regulating chromatin remodeling, transcription and other nuclear processes by acetylating histone and nonhistone proteins. This protein is a histone acetylase that has a role in DNA repair and apoptosis and is thought to play an important role in signal transduction. | Chromatin/transcription |
| KDM1A | lysine (K)-specific demethylase 1A | It is a nuclear protein containing a SWIRM domain, a FAD-binding motif, and an amine oxidase domain. This protein is a component of several histone deacetylase complexes, though it silences genes by functioning as a histone demethylase. | Chromatin/transcription |
| KDM4A | lysine (K)-specific demethylase 4A | This gene is a member of the Jumonji domain 2 (JMJD2) family and encodes a protein containing a JmjN domain, a JmjC domain, a JD2H domain, two TUDOR domains, and two PHD-type zinc fingers. This nuclear protein functions as a trimethylation-specific demethylase, converting specific trimethylated histone residues to the dimethylated form, and as a transcriptional repressor. | Chromatin/transcription |
| KDM5A | lysine (K)-specific demethylase 5A | The protein is a ubiquitously expressed nuclear protein. This protein also interacts with rhombotin-2, which functions distinctly in erythropoiesis and in T-cell leukemogenesis. Rhombotin-2 is thought to either directly affect the activity of the encoded protein or may indirectly modulate the functions of the retinoblastoma protein by binding to this protein. | Chromatin/transcription |
| KDM5B | lysine (K)-specific demethylase 5B | Histone demethylase that demethylates 'Lys-4' of histone H3, thereby playing a central role in histone code. Does not demethylate histone H3 'Lys-9' or H3 'Lys-27'. Demethylates trimethylated, dimethylated and monomethylated H3 'Lys-4'. Acts as a transcriptional corepressor for FOXG1B and PAX9. Favors the proliferation of breast cancer cells by repressing tumor suppressor genes such as BRCA1 and HOXA5. In contrast, may act as a tumor suppressor for melanoma. | Chromatin/transcription |
| L3MBTL1 | l(3)mbt-like 1 (Drosophila) | This gene represents a polycomb group gene. The encoded protein functions to regulate gene activity, likely via chromatin modification. The encoded protein may also be necessary for mitosis. | Chromatin/transcription |
| L3MBTL2 | l(3)mbt-like 2 (Drosophila) | Same as L3MBTL1. Binds to monomethylated and dimethylated 'Lys-20' on histone H4. Binds histone H3 peptides that are monomethylated or dimethylated on 'Lys-4', 'Lys-9' or 'Lys-27'. | Chromatin/transcription |
| LDB1 | LIM domain binding 1 | Binds to the LIM domain of a wide variety of LIM domain-containing transcription factors. May regulate the transcriptional activity of LIM-containing proteins by determining specific partner interactions. May play a role in the development of motor neurons. Acts synergistically with LHX1/LIM1 in axis formation and activation of gene expression. Acts with LMO2 in the regulation of red blood cell development, maintaining erythroid precursors in an immature state | Chromatin/transcription |
| LIN54 | lin-54 homolog (C. elegans) | LIN54 is a component of the LIN, or DREAM, complex, an essential regulator of cell cycle genes | G1/S and G2/M cell cycle progression/meiosis |
| LIN9 | lin-9 homolog (C. elegans) | LIN9 is a component of the LIN, or DREAM, complex, an essential regulator of cell cycle genes | G1/S and G2/M cell cycle progression/meiosis |
| LMNA | lamin A/C | The nuclear lamina consists of a two-dimensional matrix of proteins located next to the inner nuclear membrane. The lamin family of proteins make up the matrix and are highly conserved in evolution. During mitosis, the lamina matrix is reversibly disassembled as the lamin proteins are phosphorylated. Lamin proteins are thought to be involved in nuclear stability, chromatin structure and gene expression. | Chromatin/transcription |
| LMO2 | LIM domain only 2 (rhombotin- | LMO2 encodes a cysteine-rich, two LIM-domain protein that is required for yolk sac erythropoiesis. The LMO2 protein has a central and crucial role in hematopoietic development and is highly conserved. The LMO2 | Chromatin/transcription |

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| | like 1) | transcription start site is located approximately 25 kb downstream from the 11p13 T-cell translocation cluster (11p13 ttc), where a number T-cell acute lymphoblastic leukemia-specific translocations occur. | |
| MAPK14 | mitogen-activated protein kinase 14 | The protein is a member of the MAP kinase family. The activation requires its phosphorylation by MAP kinase kinases (MKKs), or its autophosphorylation triggered by the interaction of MAP3K7IP1/TAB1 protein with this kinase. The substrates of this kinase include transcription regulator ATF2, MEF2C, and MAX, cell cycle regulator CDC25B, and tumor suppressor p53, which suggest the roles of this kinase in stress related transcription and cell cycle regulation, as well as in genotoxic stress response. | Cell Differentiation |
| MCM7 | minichromosome maintenance complex component 7 | The hexameric protein complex formed by the MCM proteins is a key component of the pre-replication complex (pre_RC) and may be involved in the formation of replication forks and in the recruitment of other DNA replication related proteins. The MCM complex consisting of this protein and MCM2, 4 and 6 proteins possesses DNA helicase activity, and may act as a DNA unwinding enzyme. Cyclin D1-dependent kinase, CDK4, is found to associate with this protein, and may regulate the binding of this protein with the tumorsuppressor protein RB1/RB. | DNA replication/repair/HR/cohesion |
| MDM2 | Mdm2, p53 E3 ubiquitin protein ligase homolog (mouse) | This gene is a target gene of the transcription factor tumor protein p53. The encoded protein is a nuclear phosphoprotein that binds and inhibits transactivation by tumor protein p53, as part of an autoregulatory negative feedback loop. Overexpression of this gene can result in excessive inactivation of tumor protein p53, diminishing its tumor suppressor function. This protein has E3 ubiquitin ligase activity, which targets tumor protein p53 for proteasomal degradation. This protein also affects the cell cycle, apoptosis, and tumorigenesis through interactions with other proteins, including retinoblastoma 1 and ribosomal protein L5. | protein degradation/ proteasome |
| MNAT1 | menage a trois homolog 1, cyclin H assembly factor | The protein encoded by this gene, along with cyclin H and CDK7, forms the CDK-activating kinase (CAK) enzymatic complex. This complex activates several cyclin-associated kinases and can also associate with TFIIH to activate transcription by RNA polymerase II. | G1/S and G2/M cell cycle progression/meiosis |
| MORF4L1 | mortality factor 4 like 1 | Component of the NuA4 histone acetyltransferase (HAT) complex, which is involved in transcriptional activation of select genes principally by acetylation of nucleosomal histones H4 and H2A. This modification may both alter nucleosome - DNA interactions and promote interaction of the modified histones with other proteins, which positively regulate transcription. This complex may be required for the activation of transcriptional programs associated with oncogene and proto-oncogene mediated growth induction, tumor suppressor mediated growth arrest and replicative senescence, apoptosis, and DNA repair. | Chromatin/transcription |
| MORF4L2 | mortality factor 4 like 2 | Same as MORF4L1. | Chromatin/transcription |
| MRFAP1 | Morf4 family associated protein 1 | Found in a complex composed of MORF4L1, MRFAP1 and RB1. Interacts via its N-terminus with MORF4L1. Interacts with CSTB and MORF4L2. | Chromatin/transcription |
| MYC | v-myc myelocytomatosis viral oncogene homolog (avian) | The protein encoded by this gene is a multifunctional, nuclear phosphoprotein that plays a role in cell cycle progression, apoptosis and cellular transformation. It functions as a transcription factor that regulates transcription of specific target genes. Mutations, overexpression, rearrangement and translocation of this gene have been associated with a variety of hematopoietic tumors, leukemias and lymphomas, including Burkitt lymphoma. | Chromatin/transcription |
| MYOD1 | myogenic differentiation 1 | It is a nuclear protein belonging to the basic helix-loop-helix family of transcription factors and the myogenic factors subfamily. It regulates muscle cell differentiation by inducing cell cycle arrest, a prerequisite for myogenic initiation. The protein is also involved in muscle regeneration. It activates its own transcription, which may stabilize | Cell Differentiation |

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| | | commitment to myogenesis. | |
| NCOA6 | nuclear receptor coactivator 6 | The protein encoded by this gene is a transcriptional coactivator that can interact with nuclear hormone receptors to enhance their transcriptional activator functions. This protein has been shown to be involved in the hormone-dependent coactivation of several receptors, including prostanoid, retinoid, vitamin D3, thyroid hormone, and steroid receptors. | Chromatin/transcription |
| NFIX | nuclear factor I/X (CCAAT-binding transcription factor) | Recognizes and binds the palindromic sequence 5'-TTGGCNNNNNGCCAA-3' present in viral and cellular promoters and in the origin of replication of adenovirus type 2. These proteins are individually capable of activating transcription and replication. | DNA replication/repair/HR/cohesion |
| NPM1 | nucleophosmin (nucleolar phosphoprotein B23, numatrin) | It is a phosphoprotein which moves between the nucleus and the cytoplasm. The gene product is thought to be involved in several processes including regulation of the ARF/p53 pathway. A number of genes are fusion partners have been characterized, in particular the anaplastic lymphoma kinase gene on chromosome 2. Mutations in this gene are associated with acute myeloid leukemia. | Chromatin/transcription |
| PA2G4 | proliferation-associated 2G4, 38kDa | It is an RNA-binding protein involved in growth regulation. This protein is present in pre-ribosomal ribonucleoprotein complexes and may be involved in ribosome assembly and the regulation of intermediate and late steps of rRNA processing. This protein can interact with the cytoplasmic domain of the ErbB3 receptor and may contribute to transducing growth regulatory signals. This protein is also a transcriptional co-repressor of androgen receptor-regulated genes and other cell cycle regulatory genes through its interactions with histone deacetylases. This protein has been implicated in growth inhibition and the induction of differentiation of human cancer cells. | G1/S and G2/M cell cycle progression/meiosis |
| PAX6 | paired box 6 | The protein contains a homeo box domain. Both domains are known to bind DNA, and function as regulators of gene transcription. This gene is expressed in the developing nervous system, and in developing eyes. Mutations in this gene are known to cause ocular disorders such as aniridia and Peter's anomaly. | Cell Differentiation |
| PELP1 | proline, glutamate and leucine rich protein 1 | It is a transcription factor that coactivates transcription of estrogen receptor responsive genes and corepresses genes activated by other hormone receptors or sequence-specific transcription factors. Expression of this gene is regulated by both members of the estrogen receptor family. | Chromatin/transcription |
| PHB | prohibitin | Prohibitin is an evolutionarily conserved gene that is ubiquitously expressed. It is thought to be a negative regulator of cell proliferation and may be a tumor suppressor. Mutations in PHB have been linked to sporadic breast cancer. Prohibitin is expressed as two transcripts with varying lengths of 3' untranslated region. The longer transcript is present at higher levels in proliferating tissues and cells, suggesting that this longer 3' untranslated region may function as a trans-acting regulatory RNA. | DNA replication/repair/HR/cohesion |
| PIK3R3 | phosphoinositide-3-kinase, regulatory subunit 3 (gamma) | Binds to activated (phosphorylated) protein-tyrosine kinases through its SH2 domain and regulates their kinase activity. During insulin stimulation, it also binds to IRS-1. | Metabolism/mitochondria |
| PML | promyelocytic leukemia | The protein encoded by this gene is a member of the tripartite motif (TRIM) family. The TRIM motif includes three zinc-binding domains, a RING, a B-box type 1 and a B-box type 2, and a coiled-coil region. This phosphoprotein localizes to nuclear bodies where it functions as a transcription factor and tumor suppressor. Its expression is cell-cycle related and it regulates the p53 response to oncogenic signals. The gene is often involved in the translocation with the retinoic acid receptor alpha gene associated with acute promyelocytic leukemia (APL). | signaling/stress response |
| POLA1 | polymerase (DNA directed), | It is the catalytic subunit of DNA polymerase, which together with a regulatory and two primase subunits, forms the DNA polymerase alpha complex. The catalytic subunit plays an essential role in the initiation of | DNA replication/repair/HR/ |

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| | alpha 1, catalytic subunit | DNA replication. | cohesion |
| PPA1 | pyrophosphatase (inorganic) 1 | The protein encoded by this gene is a member of the inorganic pyrophosphatase (PPase) family. PPases catalyze the hydrolysis of pyrophosphate to inorganic phosphate, which is important for the phosphate metabolism of cells. | Metabolism/ mitochondria |
| PPARG | peroxisome proliferator-activated receptor gamma | It is a member of the peroxisome proliferator-activated receptor (PPAR) subfamily of nuclear receptors. PPARs form heterodimers with retinoid X receptors (RXRs) and these heterodimers regulate transcription of various genes. Three subtypes of PPARs are known: PPAR-alpha, PPAR-delta, and PPAR-gamma. The protein encoded by this gene is PPAR-gamma and is a regulator of adipocyte differentiation. Additionally, PPAR-gamma has been implicated in the pathology of numerous diseases including obesity, diabetes, atherosclerosis and cancer. | Cell Differentiation |
| PPP1CA | protein phosphatase 1, catalytic subunit, alpha isozyme | The protein encoded by this gene is one of the three catalytic subunits of protein phosphatase 1 (PP1). PP1 is a serine/threonine specific protein phosphatase known to be involved in the regulation of a variety of cellular processes, such as cell division, glycogen metabolism, muscle contractility, protein synthesis, and HIV-1 viral transcription. Increased PP1 activity has been observed in the end stage of heart failure. Studies in both human and mice suggest that PP1 is an important regulator of cardiac function. Mouse studies also suggest that PP1 functions as a suppressor of learning and memory. | Metabolism/ mitochondria |
| PRDM2 | PR domain containing 2, with ZNF domain | This tumor suppressor gene is a member of a nuclear histone/protein methyltransferase superfamily. It encodes a zinc finger protein that can bind to retinoblastoma protein, estrogen receptor, and the TPA-responsive element (MTE) of the heme-oxygenase-1 gene. Although the functions of this protein have not been fully characterized, it may (1) play a role in transcriptional regulation during neuronal differentiation and pathogenesis of retinoblastoma, (2) act as a transcriptional activator of the heme-oxygenase-1 gene, and (3) be a specific effector of estrogen action. | Chromatin/ transcription |
| PRKRA | protein kinase, interferon-inducible double stranded RNA dependent activator | It is a protein kinase activated by double-stranded RNA which mediates the effects of interferon in response to viral infection. Mutations in this gene have been associated with dystonia. | Immune Response |
| PSMA7 | proteasome (prosome, macropain) subunit, alpha type, 7 | The proteasome is a multicatalytic proteinase complex with a highly ordered ring-shaped 20S core structure. The core structure is composed of 4 rings of 28 non-identical subunits; 2 rings are composed of 7 alpha subunits and 2 rings are composed of 7 beta subunits. Proteasomes are distributed throughout eukaryotic cells at a high concentration and cleave peptides in an ATP/ubiquitin-dependent process in a non-lysosomal pathway. An essential function of a modified proteasome, the immunoproteasome, is the processing of class I MHC peptides. The core alpha subunit is also involved in regulating the hypoxia-inducible factor-1alpha, a transcription factor important for cellular responses to oxygen tension. | Protein degradation/ proteasome |
| PSMD10 | proteasome (prosome, macropain) 26S subunit, non-ATPase, 10 | It is a subunit of the PA700/19S complex, which is the regulatory component of the 26S proteasome. The 26S proteasome complex is required for ubiquitin-dependent protein degradation. This protein is a non-ATPase subunit that may be involved in protein-protein interactions. Aberrant expression of this gene may play a role in tumorigenesis. | Protein degradation/ proteasome |
| RAF1 | v-raf-1 murine leukemia viral oncogene | This gene is the cellular homolog of viral raf gene (v-raf). The encoded protein is a MAP kinase kinase kinase (MAP3K). Once activated, the cellular RAF1 protein can phosphorylate to activate the dual specificity | signaling/stress response |

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| | homolog 1 | protein kinases MEK1 and MEK2, which in turn phosphorylate to activate the serine/threonine specific protein kinases, ERK1 and ERK2. Activated ERKs are pleiotropic effectors of cell physiology and play an important role in the control of gene expression involved in the cell division cycle, apoptosis, cell differentiation and cell migration. Mutations in this gene are associated with Noonan syndrome 5 and LEOPARD syndrome 2. | |
| RBBP4 | retinoblastoma binding protein 4 | It is a ubiquitously expressed nuclear protein which belongs to a highly conserved subfamily of WD-repeat proteins. It is present in protein complexes involved in histone acetylation and chromatin assembly. It is part of the Mi-2 complex which has been implicated in chromatin remodeling and transcriptional repression associated with histone deacetylation. This encoded protein is also part of co-repressor complexes, which is an integral component of transcriptional silencing. It is found among several cellular proteins that bind directly to retinoblastoma protein to regulate cell proliferation. This protein also seems to be involved in transcriptional repression of E2F-responsive genes. | Chromatin/ transcription |
| RBBP5 | retinoblastoma binding protein 5 | It is a ubiquitously expressed nuclear protein which belongs to a highly conserved subfamily of WD-repeat proteins. The encoded protein binds directly to retinoblastoma protein, which regulates cell proliferation. It interacts preferentially with the underphosphorylated retinoblastoma protein via the E1A-binding pocket B. | Chromatin/ transcription |
| RBBP7 | retinoblastoma binding protein 7 | This protein is a ubiquitously expressed nuclear protein and belongs to a highly conserved subfamily of WD-repeat proteins. It is found among several proteins that binds directly to retinoblastoma protein, which regulates cell proliferation. The encoded protein is found in many histone deacetylase complexes, including mSin3 co-repressor complex. It is also present in protein complexes involved in chromatin assembly. This protein can interact with BRCA1 tumor-suppressor gene and may have a role in the regulation of cell proliferation and differentiation. | Chromatin/ transcription |
| RBBP8 | retinoblastoma binding protein 8 | The protein encoded by this gene is a ubiquitously expressed nuclear protein. It is found among several proteins that bind directly to pRb. This protein complexes with transcriptional co-repressor CTBP. It is also associated with BRCA1 and is thought to modulate the functions of BRCA1 in transcriptional regulation, DNA repair, and/or cell cycle checkpoint control. It is suggested that this gene may itself be a tumor suppressor acting in the same pathway as BRCA1. Three transcript variants encoding two different isoforms have been found for this gene. More transcript variants exist, but their full-length natures have not been determined. | DNA replication/ repair/HR/ cohesion |
| RBBP9 | retinoblastoma binding protein 9 | The protein encoded by this gene is a retinoblastoma binding protein that may play a role in the regulation of cell proliferation and differentiation. | Cell Differentiation |
| RBL1 | retinoblastoma-like 1 (p107) | The protein encoded by this gene is similar in sequence and possibly function to the product of the retinoblastoma 1 (RB1) gene. The RB1 gene product is a tumor suppressor protein that appears to be involved in cell cycle regulation, as it is phosphorylated in the S to M phase transition and is dephosphorylated in the G1 phase of the cell cycle. Both the RB1 protein and the product of this gene can form a complex with adenovirus E1A protein and SV40 large T-antigen, with the SV40 large T-antigen binding only to the unphosphorylated form of each protein. In addition, both proteins can inhibit the transcription of cell cycle genes containing E2F binding sites in their promoters. Due to the sequence and biochemical similarities with the RB1 protein, it is thought that the protein encoded by this gene may also be a tumor suppressor. | G1/S and G2/M cell cycle progression/ meiosis |
| RBL2 | retinoblastoma-like 2 (p130) | Directly involved in heterochromatin formation by maintaining overall chromatin structure and, in particular, that of constitutive heterochromatin by stabilizing histone methylation. Recruits and targets histone methyltransferases SUV420H1 and SUV420H2, leading to epigenetic transcriptional repression. Controls histone H4 'Lys-20' | G1/S and G2/M cell cycle progression/ meiosis |

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| | | trimethylation. Probably acts as a transcription repressor by recruiting chromatin-modifying enzymes to promoters. Potent inhibitor of E2F-mediated trans-activation, associates preferentially with E2F5 | |
| RFC1 | replication factor C (activator 1) 1, 145kDa | It is the large subunit of replication factor C, a five subunit DNA polymerase accessory protein, which is a DNA-dependent ATPase required for eukaryotic DNA replication and repair. The large subunit acts as an activator of DNA polymerases, binds to the 3' end of primers, and promotes coordinated synthesis of both strands. It may also have a role in telomere stability. | DNA replication/repair/HR/cohesion |
| RING1 | ring finger protein 1 | This gene belongs to the RING finger family, members of which encode proteins characterized by a RING domain, a zinc-binding motif related to the zinc finger domain. The gene product can bind DNA and can act as a transcriptional repressor. It is associated with the multimeric polycomb group protein complex. The gene product interacts with the polycomb group proteins BMI1, EDR1, and CBX4, and colocalizes with these proteins in large nuclear domains. It interacts with the CBX4 protein via its glycine-rich C-terminal domain. The gene maps to the HLA class II region, where it is contiguous with the RING finger genes FABGL and HKE4. | Protein degradation/proteosome |
| RNF40 | ring finger protein 40, E3 ubiquitin protein ligase | The protein encoded by this gene contains a RING finger, a motif known to be involved in protein-protein and protein-DNA interactions. This protein was reported to interact with the tumor suppressor protein RB1. Studies of the rat counterpart suggested that this protein may function as an E3 ubiquitin-protein ligase, and facilitate the ubiquitination and degradation of syntaxin 1, which is an essential component of the neurotransmitter release machinery. | Protein degradation/proteosome |
| SERPINB2 | serpin peptidase inhibitor, clade B (ovalbumin), member 2 | Inhibits urokinase-type plasminogen activator. The monocyte derived PAI-2 is distinct from the endothelial cell-derived PAI-1. | Apoptosis |
| SIRT1 | sirtuin 1 | It is a member of the sirtuin family of proteins, homologs to the yeast Sir2 protein. Members of the sirtuin family are characterized by a sirtuin core domain and grouped into four classes. The functions of human sirtuins have not yet been determined; Studies suggest that the human sirtuins may function as intracellular regulatory proteins with mono-ADP-ribosyltransferase activity. The protein encoded by this gene is included in class I of the sirtuin family. | Unknown |
| SKI | v-ski sarcoma viral oncogene homolog (avian) | It is the nuclear protooncogene protein homolog of avian sarcoma viral (v-ski) oncogene. It functions as a repressor of TGF-beta signaling, and may play a role in neural tube development and muscle differentiation. | Cell Differentiation |
| SKIL | SKI-like oncogene | The protein encoded by this gene is a component of the SMAD pathway, which regulates cell growth and differentiation through transforming growth factor-beta (TGFB). In the absence of ligand, the encoded protein binds to the promoter region of TGFB-responsive genes and recruits a nuclear repressor complex. TGFB signaling causes SMAD3 to enter the nucleus and degrade this protein, allowing these genes to be activated. | Cell Differentiation |
| SKP2 | S-phase kinase-associated protein 2, E3 ubiquitin protein ligase | It is a member of the F-box protein family which is characterized by an approximately 40 amino acid motif, the F-box. The F-box proteins constitute one of the four subunits of ubiquitin protein ligase complex called SCFs (SKP1-cullin-F-box), which function in phosphorylation-dependent ubiquitination. The F-box proteins are divided into 3 classes: Fbws containing WD-40 domains, Fbls containing leucine-rich repeats, and Fbxs containing either different protein-protein interaction modules or no recognizable motifs. The protein encoded by this gene belongs to the Fbls class; in addition to an F-box, this protein contains 10 tandem leucine-rich repeats. This protein is an essential element of the cyclin A-CDK2 S-phase kinase. It specifically recognizes phosphorylated cyclin-dependent kinase inhibitor 1B (CDKN1B, also referred to as p27 or | protein degradation/proteosome |

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| | | KIP1) predominantly in S phase and interacts with S-phase kinase-associated protein 1 (SKP1 or p19). In addition, this gene is established as a protooncogene causally involved in the pathogenesis of lymphomas. | |
| SMYD2 | SET and MYND domain containing 2 | SET domain-containing proteins, such as SMYD2, catalyze lysine methylation. | Chromatin/transcription |
| SNAPC1 | small nuclear RNA activating complex, polypeptide 1, 43kDa | Part of the SNAPc complex required for the transcription of both RNA polymerase II and III small-nuclear RNA genes. Binds to the proximal sequence element (PSE), a non-TATA-box basal promoter element common to these 2 types of genes. Recruits TBP and BRF2 to the U6 snRNA TATA box. | Chromatin/transcription |
| SNAPC3 | small nuclear RNA activating complex, polypeptide 3, 50kDa | Same as SNAPC1. | Chromatin/transcription |
| SNW1 | SNW domain containing 1 | This coactivator can bind to the ligand-binding domain of the vitamin D receptor and to retinoid receptors to enhance vitamin D-, retinoic acid-, estrogen-, and glucocorticoid-mediated gene expression. It can also function as a splicing factor by interacting with poly(A)-binding protein 2 to directly control the expression of muscle-specific genes at the transcriptional level. Finally, the protein may be involved in oncogenesis since it interacts with a region of SKI oncoproteins that is required for transforming activity. | RNA processing |
| SP1 | Sp1 transcription factor | The protein is a zinc finger transcription factor that binds to GC-rich motifs of many promoters. The encoded protein is involved in many cellular processes, including cell differentiation, cell growth, apoptosis, immune responses, response to DNA damage, and chromatin remodeling. | Immune Response |
| STAT3 | signal transducer and activator of transcription 3 (acute-phase response factor) | The protein is a member of the STAT protein family. In response to cytokines and growth factors, STAT family members are phosphorylated by the receptor associated kinases, and then form homo- or heterodimers that translocate to the cell nucleus where they act as transcription activators. This protein is activated through phosphorylation in response to various cytokines and growth factors including IFNs, EGF, IL5, IL6, HGF, LIF and BMP2. This protein mediates the expression of a variety of genes in response to cell stimuli, and thus plays a key role in many cellular processes such as cell growth and apoptosis. The small GTPase Rac1 has been shown to bind and regulate the activity of this protein. PIAS3 protein is a specific inhibitor of this protein. | Immune Response |
| SUV39H1 | suppressor of variegation 3-9 homolog 1 (Drosophila) | This gene is a member of the suppressor of variegation 3-9 homolog family and encodes a protein with a chromodomain and a C-terminal SET domain. This nuclear protein moves to the centromeres during mitosis and functions as a histone methyltransferase, methylating Lys-9 of histone H3. Overall, it plays a vital role in heterochromatin organization, chromosome segregation, and mitotic progression. | Chromatin/transcription |
| TAF1 | TAF1 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 250kDa | TFIID is composed of the TATA-binding protein (TBP) and a group of evolutionarily conserved proteins known as TBP-associated factors or TAFs. TAFs may participate in basal transcription, serve as coactivators, function in promoter recognition or modify general transcription factors (GTFs) to facilitate complex assembly and transcription initiation. It is the largest subunit of TFIID. This subunit binds to core promoter sequences encompassing the transcription start site. It also binds to activators and other transcriptional regulators, and these interactions affect the rate of transcription initiation. This subunit contains two independent protein kinase domains at the N and C-terminals, but also possesses acetyltransferase activity and can act as a ubiquitin-activating/conjugating enzyme. This gene is part of a complex | G1/S and G2/M cell cycle progression/meiosis |

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| | | transcriptional unit (TAF1/DYT3), wherein some products share exons with TAF1 as well as additional exons downstream. | |
| TAL1 | T-cell acute lymphocytic leukemia 1 | Implicated in the genesis of hemopoietic malignancies. It may play an important role in hemopoietic differentiation. Serves as a positive regulator of erythroid differentiation | Cell Differentiation |
| TBP | TATA box binding protein | It is TBP, the TATA-binding protein. A distinctive feature of TBP is a long string of glutamines in the N-terminus. This region of the protein modulates the DNA binding activity of the C terminus, and modulation of DNA binding affects the rate of transcription complex formation and initiation of transcription. The number of CAG repeats encoding the polyglutamine tract is usually 32-39, and expansion of the number of repeats increases the length of the polyglutamine string and is associated with spinocerebellar ataxia 17, a neurodegenerative disorder classified as a polyglutamine disease. | Chromatin/transcription |
| TCF3 | transcription factor 3 (E2A immunoglobulin enhancer binding factors E12/E47) | It is a member of the E protein (class I) family of helix-loop-helix transcription factors. E proteins activate transcription by binding to regulatory E-box sequences on target genes as heterodimers or homodimers, and are inhibited by heterodimerization with inhibitor of DNA-binding (class IV) helix-loop-helix proteins. E proteins play a critical role in lymphopoiesis, and the encoded protein is required for B and T lymphocyte development. Deletion of this gene or diminished activity of the encoded protein may play a role in lymphoid malignancies. This gene is also involved in several chromosomal translocations that are associated with lymphoid malignancies including pre-B-cell acute lymphoblastic leukemia (t(1;19), with PBX1), childhood leukemia (t(19;19), with TFPT) and acute leukemia (t(12;19), with ZNF384). | Chromatin/transcription |
| TFDP1 | transcription factor Dp-1 | It is a member of a family of transcription factors that heterodimerize with E2F proteins to enhance their DNA-binding activity and promote transcription from E2F target genes. The encoded protein functions as part of this complex to control the transcriptional activity of numerous genes involved in cell cycle progression from G1 to S phase. | G1/S and G2/M cell cycle progression/meiosis |
| TFDP2 | transcription factor Dp-2 (E2F dimerization partner 2) | The gene is a member of the transcription factor DP family. The encoded protein forms heterodimers with the E2F transcription factors resulting in transcriptional activation of cell cycle regulated genes. | G1/S and G2/M cell cycle progression/meiosis |
| TGM2 | transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferrase) | Transglutaminases are enzymes that catalyze the crosslinking of proteins by epsilon-gamma glutamyl lysine isopeptide bonds. While the primary structure of transglutaminases is not conserved, they all have the same amino acid sequence at their active sites and their activity is calcium-dependent. The protein acts as a monomer, is induced by retinoic acid, and appears to be involved in apoptosis. | Apoptosis |
| THOC1 | THO complex 1 | Component of the THO subcomplex of the TREX complex. The TREX complex specifically associates with spliced mRNA and not with unspliced pre-mRNA. It is recruited to spliced mRNAs by a transcription-independent mechanism. Binds to mRNA upstream of the exon-junction complex (EJC) and is recruited in a splicing- and cap-dependent manner to a region near the 5' end of the mRNA where it functions in mRNA export. | RNA processing |
| TMPO | thymopoietin | The protein encoded by this gene resides in the nucleus and may play a role in the assembly of the nuclear lamina, and thus help maintain the structural organization of the nuclear envelope. It may function as a receptor for the attachment of lamin filaments to the inner nuclear membrane. Mutations in this gene are associated with dilated cardiomyopathy. | DNA replication/repair/HR/cohesion |
| TP53 | tumor protein p53 | It is tumor protein p53, which responds to diverse cellular stresses to regulate target genes that induce cell cycle arrest, apoptosis, senescence, DNA repair, or changes in metabolism. p53 is a DNA-binding protein | Apoptosis |

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| | | containing transcription activation, DNA-binding, and oligomerization domains. It is postulated to bind to a p53-binding site and activate expression of downstream genes that inhibit growth and/or invasion, and thus function as a tumor suppressor. Mutants of p53 that frequently occur in a number of different human cancers fail to bind the consensus DNA binding site, and hence cause the loss of tumor suppressor activity. Alterations of this gene occur not only as somatic mutations in human malignancies, but also as germline mutations in some cancer-prone families with Li-Fraumeni syndrome. | |
| TP73 | tumor protein p73 | It is a member of the p53 family of transcription factors involved in cellular responses to stress and development. It maps to a region on chromosome 1p36 that is frequently deleted in neuroblastoma and other tumors, and thought to contain multiple tumor suppressor genes. The demonstration that this gene is monoallelically expressed (likely from the maternal allele), supports the notion that it is a candidate gene for neuroblastoma. | Apoptosis |
| TRAP1 | TNF receptor-associated protein 1 | HSP90 proteins are highly conserved molecular chaperones that have key roles in signal transduction, protein folding, protein degradation, and morphologic evolution. HSP90 proteins normally associate with other cochaperones and play important roles in folding newly synthesized proteins or stabilizing and refolding denatured proteins after stress. TRAP1 is a mitochondrial HSP90 protein. | protein folding/protein glycosylation/ cell wall biogenesis & integrity |
| TRIM27 | tripartite motif containing 27 | It is a member of the tripartite motif (TRIM) family. The TRIM motif includes three zinc-binding domains, a RING, a B-box type 1 and a B-box type 2, and a coiled-coil region. This protein localizes to the nuclear matrix. It interacts with the enhancer of polycomb protein and represses gene transcription. It is also thought to be involved in the differentiation of male germ cells. Fusion of the N-terminus of this protein with the truncated C-terminus of the RET gene product has been shown to result in production of the ret transforming protein. | Apoptosis |
| TRIP11 | thyroid hormone receptor interactor 11 | This gene was identified based on the interaction of its protein product with thyroid hormone receptor beta. This protein is associated with the Golgi apparatus. The N-terminal region of the protein binds Golgi membranes and the C-terminal region binds the minus ends of microtubules; thus, the protein is thought to play a role in assembly and maintenance of the Golgi ribbon structure around the centrosome. Mutations in this gene cause achondrogenesis type IA. | Golgi/endosome /vacuole/sorting |
| UBC | ubiquitin C | This gene represents a ubiquitin gene, ubiquitin C. The encoded protein is a polyubiquitin precursor. Conjugation of ubiquitin monomers or polymers can lead to various effects within a cell, depending on the residues to which ubiquitin is conjugated. Ubiquitination has been associated with protein degradation, DNA repair, cell cycle regulation, kinase modification, endocytosis, and regulation of other cell signaling pathways. | Protein degradation/ proteosome |
| UBR4 | ubiquitin protein ligase E3 component n-recognin 4 | The protein encoded by this gene is an E3 ubiquitin-protein ligase that interacts with the retinoblastoma-associated protein in the nucleus and with calcium-bound calmodulin in the cytoplasm. The encoded protein appears to be a cytoskeletal component in the cytoplasm and part of the chromatin scaffold in the nucleus. In addition, this protein is a target of the human papillomavirus type 16 E7 oncoprotein. | Protein degradation/ proteosome |
| UBTF | upstream binding transcription factor, RNA polymerase I | It is a member of the HMG-box DNA-binding protein family. The encoded protein plays a critical role in ribosomal RNA transcription as a key component of the pre-initiation complex, mediating the recruitment of RNA polymerase I to rDNA promoter regions. The encoded protein may also play important roles in chromatin remodeling and pre-rRNA processing, and its activity is regulated by both phosphorylation and acetylation. | Chromatin/transcription |
| UHRF1 | ubiquitin-like with PHD and ring finger domains 1 | It is a member of a subfamily of RING-finger type E3 ubiquitin ligases. The protein binds to specific DNA sequences, and recruits a histone deacetylase to regulate gene expression. Its expression peaks at late G1 phase and continues during G2 and M phases of the cell cycle. It plays a | Protein degradation/ proteosome |

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| | | major role in the G1/S transition by regulating topoisomerase IIalpha and retinoblastoma gene expression, and functions in the p53-dependent DNA damage checkpoint. Multiple transcript variants encoding different isoforms have been found for this gene. | |
| UHRF2 | ubiquitin-like with PHD and ring finger domains 2, E3 ubiquitin protein ligase | It is a nuclear protein which is involved in cell-cycle regulation. The encoded protein is a ubiquitin-ligase capable of ubiquitinating PCNP (PEST-containing nuclear protein), and together they may play a role in tumorigenesis. The encoded protein contains an NIRF_N domain, a PHD finger, a set- and ring-associated (SRA) domain, and a RING finger domain and several of these domains have been shown to be essential for the regulation of cell proliferation. This protein may also have a role in intranuclear degradation of polyglutamine aggregates. | Protein degradation/ proteosome |
| USP4 | ubiquitin specific peptidase 4 (proto-oncogene) | The protein encoded by this gene is a protease that deubiquitinates target proteins such as ADORA2A and TRIM21. The encoded protein shuttles between the nucleus and cytoplasm and is involved in maintaining operational fidelity in the endoplasmic reticulum. | Protein degradation/ proteosome |
| VDR | vitamin D (1,25-dihydroxyvitamin D3) receptor | It is the nuclear hormone receptor for vitamin D3. This receptor also functions as a receptor for the secondary bile acid lithocholic acid. The receptor belongs to the family of trans-acting transcriptional regulatory factors and shows sequence similarity to the steroid and thyroid hormone receptors. Downstream targets of this nuclear hormone receptor are principally involved in mineral metabolism though the receptor regulates a variety of other metabolic pathways, such as those involved in the immune response and cancer. Mutations in this gene are associated with type II vitamin D-resistant rickets. A single nucleotide polymorphism in the initiation codon results in an alternate translation start site three codons downstream. | Chromatin/ transcription |
| YY1 | YY1 transcription factor | YY1 is a ubiquitously distributed transcription factor belonging to the GLI-Kruppel class of zinc finger proteins. The protein is involved in repressing and activating a diverse number of promoters. YY1 may direct histone deacetylases and histone acetyltransferases to a promoter in order to activate or repress the promoter, thus implicating histone modification in the function of YY1. | Cell Differentiation |
| ZBTB7A | zinc finger and BTB domain containing 7A | Unknown | Unknown |
| AP1AR | adaptor-related protein complex 1 associated regulatory protein | Necessary for AP-1 dependent transport between the trans-Golgi network and endosomes. Regulates the membrane association of AP1G1/Gamma1-adaptin, one of the subunits of the AP-1 adapter complex. The direct interaction with AP1G1/Gamma1-adaptin attenuates the release of the AP-1 complex from membranes. | Golgi/endosome /vacuole/sorting |
| BDP1 | B double prime 1, subunit of RNA polymerase III transcription initiation factor IIIB | The product of this gene is a subunit of the TFIIB transcription initiation complex, which recruits RNA polymerase III to target promoters in order to initiate transcription. The encoded protein localizes to concentrated aggregates in the nucleus, and is required for transcription from all three types of polymerase III promoters. It is phosphorylated by casein kinase II during mitosis, resulting in its release from chromatin and suppression of polymerase III transcription. | Chromatin/ transcription |
| BNC2 | basonuclin 2 | Probable transcription factor specific for skin keratinocytes. May play a role in the differentiation of spermatozoa and oocytes. | Cell Differentiation |
| BRAF | v-raf murine sarcoma viral oncogene homolog B1 | It is a protein belonging to the raf/mil family of serine/threonine protein kinases. This protein plays a role in regulating the MAP kinase/ERKs signaling pathway, which affects cell division, differentiation, and secretion. Mutations in this gene are associated with cardiofaciocutaneous syndrome, a disease characterized by heart defects, mental retardation and a distinctive facial appearance. Mutations in this gene have also been associated with various cancers, including non-Hodgkin lymphoma, colorectal cancer, malignant melanoma, thyroid | signaling/stress response |

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| | | carcinoma, non-small cell lung carcinoma, and adenocarcinoma of lung. | |
| CASP10 | caspase 10, apoptosis-related cysteine peptidase | It is a member of the cysteine-aspartic acid protease (caspase) family. Caspases exist as inactive proenzymes which undergo proteolytic processing at conserved aspartic residues to produce two subunits, large and small, that dimerize to form the active enzyme. This protein cleaves and activates caspases 3 and 7, and the protein itself is processed by caspase 8. Mutations in this gene are associated with type IIA autoimmune lymphoproliferative syndrome, non-Hodgkin lymphoma and gastric cancer. | Apoptosis |
| CASP2 | caspase 2, apoptosis-related cysteine peptidase | It is a member of the cysteine-aspartic acid protease (caspase) family. The encoded protein may function in stress-induced cell death pathways, cell cycle maintenance, and the suppression of tumorigenesis. Increased expression of this gene may play a role in neurodegenerative disorders including Alzheimer's disease, Huntington's disease and temporal lobe epilepsy. | Apoptosis |
| CASP3 | caspase 3, apoptosis-related cysteine peptidase | It is a protein which is a member of the caspase family. Caspases exist as inactive proenzymes which undergo proteolytic processing at conserved aspartic residues to produce two subunits, large and small, that dimerize to form the active enzyme. This protein cleaves and activates caspases 6, 7 and 9, and the protein itself is processed by caspases 8, 9 and 10. It is the predominant caspase involved in the cleavage of amyloid-beta 4A precursor protein, which is associated with neuronal death in Alzheimer's disease. | Apoptosis |
| CASP6 | caspase 6, apoptosis-related cysteine peptidase | It is a protein which is a member of the caspase family. Caspases exist as inactive proenzymes which undergo proteolytic processing at conserved aspartic residues to produce two subunits, large and small, that dimerize to form the active enzyme. This protein is processed by caspases 7, 8 and 10, and is thought to function as a downstream enzyme in the caspase activation cascade. | Apoptosis |
| CASP7 | caspase 7, apoptosis-related cysteine peptidase | It is a protein which is a member of the caspase family. Sequential activation of caspases plays a central role in the execution-phase of cell apoptosis. Caspases exist as inactive proenzymes which undergo proteolytic processing at conserved aspartic residues to produce two subunits, large and small, that dimerize to form the active enzyme. The precursor of this caspase is cleaved by caspase 3 and 10. It is activated upon cell death stimuli and induces apoptosis. | Apoptosis |
| CASP8 | caspase 8, apoptosis-related cysteine peptidase | It is a member of the caspase family. Activation of caspases requires proteolytic processing at conserved internal aspartic residues to generate a heterodimeric enzyme consisting of the large and small subunits. This protein is involved in the programmed cell death induced by Fas and various apoptotic stimuli. The N-terminal FADD-like death effector domain of this protein suggests that it may interact with Fas-interacting protein FADD. This protein was detected in the insoluble fraction of the affected brain region from Huntington disease patients but not in those from normal controls, which implicated the role in neurodegenerative diseases. | Apoptosis |
| CASP9 | caspase 9, apoptosis-related cysteine peptidase | It is a member of caspase family. Sequential activation of caspases plays a central role in the execution-phase of cell apoptosis. Caspases exist as inactive proenzymes which undergo proteolytic processing at conserved aspartic residues to produce two subunits, large and small, that dimerize to form the active enzyme. This protein is processed by caspase APAF1; this step is thought to be one of the earliest in the caspase activation cascade. | Apoptosis |
| CDK14 | cyclin-dependent kinase 14 | PFTK1 is a member of the CDC2-related protein kinase family. | G1/S and G2/M cell cycle progression/meiosis |
| CDKN1A | cyclin-dependent kinase inhibitor 1A | It is a potent cyclin-dependent kinase inhibitor. The encoded protein binds to and inhibits the activity of cyclin-CDK2 or -CDK4 complexes, and thus functions as a regulator of cell cycle progression at G1. The expression of this gene is tightly controlled by the tumor suppressor | G1/S and G2/M cell cycle progression/meiosis |

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| | (p21, Cip1) | protein p53, through which this protein mediates the p53-dependent cell cycle G1 phase arrest in response to a variety of stress stimuli. This protein can interact with proliferating cell nuclear antigen (PCNA), a DNA polymerase accessory factor, and plays a regulatory role in S phase DNA replication and DNA damage repair. This protein was reported to be specifically cleaved by CASP3-like caspases, which thus leads to a dramatic activation of CDK2, and may be instrumental in the execution of apoptosis following caspase activation. | |
| CEBPD | CCAAT/enhancer binding protein (C/EBP), delta | The protein encoded by this intronless gene is a bZIP transcription factor which can bind as a homodimer to certain DNA regulatory regions. It can also form heterodimers with the related protein CEBP-alpha. The encoded protein is important in the regulation of genes involved in immune and inflammatory responses, and may be involved in the regulation of genes associated with activation and/or differentiation of macrophages. | Immune Response |
| CEBPE | CCAAT/enhancer binding protein (C/EBP), epsilon | The protein encoded by this gene is a bZIP transcription factor which can bind as a homodimer to certain DNA regulatory regions. It can also form heterodimers with the related protein CEBP-delta. The encoded protein may be essential for terminal differentiation and functional maturation of committed granulocyte progenitor cells. Mutations in this gene have been associated with Specific Granule Deficiency, a rare congenital disorder. | Immune Response |
| CHEK1 | checkpoint kinase 1 | The protein encoded by this gene belongs to the Ser/Thr protein kinase family. It is required for checkpoint mediated cell cycle arrest in response to DNA damage or the presence of unreplicated DNA. This protein acts to integrate signals from ATM and ATR, two cell cycle proteins involved in DNA damage responses, that also associate with chromatin in meiotic prophase I. Phosphorylation of CDC25A protein phosphatase by this protein is required for cells to delay cell cycle progression in response to double-strand DNA breaks. | DNA replication/repair/HR/cohesion |
| CHEK2 | checkpoint kinase 2 | In response to DNA damage and replication blocks, cell cycle progression is halted through the control of critical cell cycle regulators. The protein encoded by this gene is a cell cycle checkpoint regulator and putative tumor suppressor. It contains a forkhead-associated protein interaction domain essential for activation in response to DNA damage and is rapidly phosphorylated in response to replication blocks and DNA damage. When activated, the encoded protein is known to inhibit CDC25C phosphatase, preventing entry into mitosis, and has been shown to stabilize the tumor suppressor protein p53, leading to cell cycle arrest in G1. In addition, this protein interacts with and phosphorylates BRCA1, allowing BRCA1 to restore survival after DNA damage. Mutations in this gene have been linked with Li-Fraumeni syndrome, a highly penetrant familial cancer phenotype usually associated with inherited mutations in TP53. Also, mutations in this gene are thought to confer a predisposition to sarcomas, breast cancer, and brain tumors. This nuclear protein is a member of the CDS1 subfamily of serine/threonine protein kinases. | DNA replication/repair/HR/cohesion |
| CTBP1 | C-terminal binding protein 1 | It is a protein that binds to the C-terminus of adenovirus E1A proteins. This phosphoprotein is a transcriptional repressor and may play a role during cellular proliferation. This protein and the product of a second closely related gene, CTBP2, can dimerize. Both proteins can also interact with a polycomb group protein complex which participates in regulation of gene expression during development. | Cell Differentiation |
| DGKZ | diacylglycerol kinase, zeta | The protein belongs to the eukaryotic diacylglycerol kinase family. It may attenuate protein kinase C activity by regulating diacylglycerol levels in intracellular signaling cascade and signal transduction. | Metabolism/mitochondria |
| E2F3 | E2F transcription factor 3 | Same as E2F1. | G1/S and G2/M cell cycle progression/meiosis |
| ELF1 | E74-like | It is an E26 transformation-specific related transcription factor. The | Chromatin/ |

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| | factor 1 (ets domain transcription factor) | protein is primarily expressed in lymphoid cells and acts as both an enhancer and a repressor to regulate transcription of various genes. | transcription |
| FOS | FBJ murine osteosarcoma viral oncogene homolog | The Fos gene family consists of 4 members: FOS, FOSB, FOSL1, and FOSL2. These genes encode leucine zipper proteins that can dimerize with proteins of the JUN family, thereby forming the transcription factor complex AP-1. As such, the FOS proteins have been implicated as regulators of cell proliferation, differentiation, and transformation. In some cases, expression of the FOS gene has also been associated with apoptotic cell death. | Cell Differentiation |
| GATA1 | GATA binding protein 1 (globin transcription factor 1) | It is a protein which belongs to the GATA family of transcription factors. The protein plays an important role in erythroid development by regulating the switch of fetal hemoglobin to adult hemoglobin. Mutations in this gene have been associated with X-linked dyserythropoietic anemia and thrombocytopenia. | Cell Differentiation |
| GSR | glutathione reductase | It is a member of the class-I pyridine nucleotide-disulfide oxidoreductase family. This enzyme is a homodimeric flavoprotein. It is a central enzyme of cellular antioxidant defense, and reduces oxidized glutathione disulfide (GSSG) to the sulfhydryl form GSH, which is an important cellular antioxidant. Rare mutations in this gene result in hereditary glutathione reductase deficiency. | Metabolism/ mitochondria |
| GTF3C2 | general transcription factor IIIC, polypeptide 2, beta 110kDa | Same as GTF3C1 | Chromatin/ transcription |
| HIF1A | hypoxia inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor) | It is the alpha subunit of transcription factor hypoxia-inducible factor-1 (HIF-1), which is a heterodimer composed of an alpha and a beta subunit. HIF-1 functions as a master regulator of cellular and systemic homeostatic response to hypoxia by activating transcription of many genes, including those involved in energy metabolism, angiogenesis, apoptosis, and other genes whose protein products increase oxygen delivery or facilitate metabolic adaptation to hypoxia. HIF-1 thus plays an essential role in embryonic vascularization, tumor angiogenesis and pathophysiology of ischemic disease. | Chromatin/ transcription |
| HSPA8 | heat shock 70kDa protein 8 | It is a member of the heat shock protein 70 family, which contains both heat-inducible and constitutively expressed members. This protein belongs to the latter group, which are also referred to as heat-shock cognate proteins. It functions as a chaperone, and binds to nascent polypeptides to facilitate correct folding. It also functions as an ATPase in the disassembly of clathrin-coated vesicles during transport of membrane components through the cell. | Chromatin/ transcription |
| ID2 | inhibitor of DNA binding 2, dominant negative helix-loop-helix protein | The protein encoded by this gene belongs to the inhibitor of DNA binding family, members of which are transcriptional regulators that contain a helix-loop-helix (HLH) domain but not a basic domain. Members of the inhibitor of DNA binding family inhibit the functions of basic helix-loop-helix transcription factors in a dominant-negative manner by suppressing their heterodimerization partners through the HLH domains. | Chromatin/ transcription |
| INS | insulin | After removal of the precursor signal peptide, proinsulin is post-translationally cleaved into three peptides: the B chain and A chain peptides, which are covalently linked via two disulfide bonds to form insulin, and C-peptide. Binding of insulin to the insulin receptor (INSR) stimulates glucose uptake. | Metabolism/ mitochondria |
| LIN37 | lin-37 homolog | It is a protein expressed in the eye. | G1/S and G2/M cell cycle progression/ meiosis |
| MAPK9 | mitogen- | The protein encoded by this gene is a member of the MAP kinase family. | Cell |

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| | activated protein kinase 9 | MAP kinases act as an integration point for multiple biochemical signals, and are involved in a wide variety of cellular processes such as proliferation, differentiation, transcription regulation and development. This kinase targets specific transcription factors, and thus mediates immediate-early gene expression in response to various cell stimuli. It is most closely related to MAPK8, both of which are involved in UV radiation induced apoptosis, thought to be related to the cytochrome c-mediated cell death pathway. This gene and MAPK8 are also known as c-Jun N-terminal kinases. This kinase blocks the ubiquitination of tumor suppressor p53, and thus it increases the stability of p53 in nonstressed cells. Studies of this gene's mouse counterpart suggest a key role in T-cell differentiation. | Differentiation |
| MDM4 | Mdm4 p53 binding protein homolog (mouse) | It is a nuclear protein that contains a p53 binding domain at the N-terminus and a RING finger domain at the C-terminus, and shows structural similarity to p53-binding protein MDM2. Both proteins bind the p53 tumor suppressor protein and inhibit its activity, and have been shown to be overexpressed in a variety of human cancers. However, unlike MDM2 which degrades p53, this protein inhibits p53 by binding its transcriptional activation domain. This protein also interacts with MDM2 protein via the RING finger domain, and inhibits the latter's degradation. So this protein can reverse MDM2-targeted degradation of p53, while maintaining suppression of p53 transactivation and apoptotic functions. | protein degradation/ proteasome |
| MRPS18B | mitochondrial ribosomal protein S18B | Mitochondrial ribosomes (mitoribosomes) consist of a small 28S subunit and a large 39S subunit. Among different species, the proteins comprising the mitoribosome differ greatly in sequence, and sometimes in biochemical properties, which prevents easy recognition by sequence homology. It is a 28S subunit protein that belongs to the ribosomal protein S18P family. | Metabolism/ mitochondria |
| NCL | nucleolin | Nucleolin (NCL), a eukaryotic nucleolar phosphoprotein, is involved in the synthesis and maturation of ribosomes. It is located mainly in dense fibrillar regions of the nucleolus. Human NCL gene consists of 14 exons with 13 introns and spans approximately 11kb. The intron 11 of the NCL gene encodes a small nucleolar RNA, termed U20. | RNA processing |
| NDC80 | NDC80 kinetochore complex component homolog (S. cerevisiae) | It is a component of the NDC80 kinetochore complex. The encoded protein consists of an N-terminal microtubule binding domain and a C-terminal coiled-coiled domain that interacts with other components of the complex. This protein functions to organize and stabilize microtubule-kinetochore interactions and is required for proper chromosome segregation. | Chromosome segregation/ kinetochore/ spindle/ microtubule |
| NEFM | neurofilament, medium polypeptide | Neurofilaments are type IV intermediate filament heteropolymers composed of light, medium, and heavy chains. Neurofilaments comprise the axoskeleton and functionally maintain neuronal caliber. They may also play a role in intracellular transport to axons and dendrites. It is the medium neurofilament protein. This protein is commonly used as a biomarker of neuronal damage. | Chromosome segregation/ kinetochore/ spindle/ microtubule |
| PABPN1 | poly(A) binding protein, nuclear 1 | It is an abundant nuclear protein that binds with high affinity to nascent poly(A) tails. The protein is required for progressive and efficient polymerization of poly(A) tails at the 3' ends of eukaryotic transcripts and controls the size of the poly(A) tail to about 250 nt. At steady-state, this protein is localized in the nucleus whereas a different poly(A) binding protein is localized in the cytoplasm. This gene contains a GCG trinucleotide repeat at the 5' end of the coding region, and expansion of this repeat from the normal 6 copies to 8-13 copies leads to autosomal dominant oculopharyngeal muscular dystrophy (OPMD) disease. | RNA processing |
| PAX2 | paired box 2 | The central feature of this transcription factor is the conserved DNA-binding paired box domain. PAX2 is believed to be a target of transcriptional suppression by the tumor suppressor gene WT1. Mutations within PAX2 have been shown to result in optic nerve colobomas and renal hypoplasia. | Cell Differentiation |
| PAX5 | paired box 5 | It is a member of the paired box (PAX) family of transcription factors. | Cell |

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| | | <p>The central feature of this gene family is a novel, highly conserved DNA-binding motif, known as the paired box. PAX proteins are important regulators in early development, and alterations in the expression of their genes are thought to contribute to neoplastic transformation. It is the B-cell lineage specific activator protein that is expressed at early, but not late stages of B-cell differentiation. Its expression has also been detected in developing CNS and testis and so the encoded protein may also play a role in neural development and spermatogenesis. This gene is located at 9p13, which is involved in t(9;14)(p13;q32) translocations recurring in small lymphocytic lymphomas of the plasmacytoid subtype, and in derived large-cell lymphomas. This translocation brings the potent E-mu enhancer of the IgH gene into close proximity of the PAX5 promoter, suggesting that the deregulation of transcription of this gene contributes to the pathogenesis of these lymphomas</p> | Differentiation |
| PCNA | proliferating cell nuclear antigen | <p>The protein is found in the nucleus and is a cofactor of DNA polymerase delta. The protein acts as a homotrimer and helps increase the processivity of leading strand synthesis during DNA replication. In response to DNA damage, this protein is ubiquitinated and is involved in the RAD6-dependent DNA repair pathway.</p> | DNA replication/repair/HR/cohesion |
| PIK3R1 | phosphoinositide-3-kinase, regulatory subunit 1 (alpha) | <p>Phosphatidylinositol 3-kinase phosphorylates the inositol ring of phosphatidylinositol at the 3-prime position. The enzyme comprises a 110 kD catalytic subunit and a regulatory subunit of either 85, 55, or 50 kD. It is the 85 kD regulatory subunit. Phosphatidylinositol 3-kinase plays an important role in the metabolic actions of insulin, and a mutation in this gene has been associated with insulin resistance.</p> | Metabolism/mitochondria |
| PON2 | paraoxonase 2 | <p>It is a member of the paraoxonase gene family, which includes three known members located adjacent to each other on the long arm of chromosome 7. The encoded protein is ubiquitously expressed in human tissues, membrane-bound, and may act as a cellular antioxidant, protecting cells from oxidative stress. Hydrolytic activity against acylhomoserine lactones, important bacterial quorum-sensing mediators, suggests the encoded protein may also play a role in defense responses to pathogenic bacteria. Mutations in this gene may be associated with vascular disease and a number of quantitative phenotypes related to diabetes.</p> | Metabolism/mitochondria |
| PPIA | peptidylprolyl isomerase A (cyclophilin A) | <p>It is a member of the peptidyl-prolyl cis-trans isomerase (PPIase) family. PPIases catalyze the cis-trans isomerization of proline imidic peptide bonds in oligopeptides and accelerate the folding of proteins. The encoded protein is a cyclosporin binding-protein and may play a role in cyclosporin A-mediated immunosuppression. The protein can also interact with several HIV proteins, including p55 gag, Vpr, and capsid protein, and has been shown to be necessary for the formation of infectious HIV virions.</p> | Metabolism/mitochondria |
| PPP1CB | protein phosphatase 1, catalytic subunit, beta isozyme | <p>The protein is one of the three catalytic subunits of protein phosphatase 1 (PP1). PP1 is a serine/threonine specific protein phosphatase known to be involved in the regulation of a variety of cellular processes, such as cell division, glycogen metabolism, muscle contractility, protein synthesis, and HIV-1 viral transcription. Mouse studies suggest that PP1 functions as a suppressor of learning and memory.</p> | Metabolism/mitochondria |
| PPP1CC | protein phosphatase 1, catalytic subunit, gamma isozyme | <p>The protein belongs to the protein phosphatase family, PP1 subfamily. PP1 is an ubiquitous serine/threonine phosphatase that regulates many cellular processes, including cell division. It is expressed in mammalian cells as three closely related isoforms, alpha, beta/delta and gamma, which have distinct localization patterns. It is the gamma isozyme.</p> | Metabolism/mitochondria |
| PRKCB | protein kinase C, beta | <p>Protein kinase C (PKC) is a family of serine- and threonine-specific protein kinases that can be activated by calcium and second messenger diacylglycerol. PKC family members phosphorylate a wide variety of protein targets and are known to be involved in diverse cellular signaling pathways. PKC family members also serve as major receptors for</p> | Metabolism/mitochondria |

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| | | phorbol esters, a class of tumor promoters. Each member of the PKC family has a specific expression profile and is believed to play a distinct role in cells. The protein encoded by this gene is one of the PKC family members. This protein kinase has been reported to be involved in many different cellular functions, such as B cell activation, apoptosis induction, endothelial cell proliferation, and intestinal sugar absorption. Studies in mice also suggest that this kinase may also regulate neuronal functions and correlate fear-induced conflict behavior after stress. | |
| PRMT2 | protein arginine methyltransferase 2 | | Chromatin/transcription |
| PSMC4 | proteasome (prosome, macropain) 26S subunit, ATPase, 4 | The 26S proteasome is a multicatalytic proteinase complex with a highly ordered structure composed of 2 complexes, a 20S core and a 19S regulator. The 20S core is composed of 4 rings of 28 non-identical subunits; 2 rings are composed of 7 alpha subunits and 2 rings are composed of 7 beta subunits. The 19S regulator is composed of a base, which contains 6 ATPase subunits and 2 non-ATPase subunits, and a lid, which contains up to 10 non-ATPase subunits. Proteasomes are distributed throughout eukaryotic cells at a high concentration and cleave peptides in an ATP/ubiquitin-dependent process in a non-lysosomal pathway. An essential function of a modified proteasome, the immunoproteasome, is the processing of class I MHC peptides. It is one of the ATPase subunits, a member of the triple-A family of ATPases which have a chaperone-like activity. This subunit has been shown to interact with an orphan member of the nuclear hormone receptor superfamily highly expressed in liver, and with gankyrin, a liver oncoprotein. | protein degradation/proteasome |
| PURA | purine-rich element binding protein A | This gene product is a sequence-specific, single-stranded DNA-binding protein. It binds preferentially to the single strand of the purine-rich element termed PUR, which is present at origins of replication and in gene flanking regions in a variety of eukaryotes from yeasts through humans. Thus, it is implicated in the control of both DNA replication and transcription. Deletion of this gene has been associated with myelodysplastic syndrome and acute myelogenous leukemia. | Chromatin/transcription |
| RBAK | RB-associated KRAB zinc finger | It is a nuclear protein which interacts with the tumor suppressor retinoblastoma 1. The two interacting proteins are thought to act as a transcriptional repressor for promoters which are activated by the E2F1 transcription factor. This protein contains a Kruppel-associated box (KRAB), which is a transcriptional repressor motif. | Chromatin/transcription |
| RUNX2 | runt-related transcription factor 2 | The protein is a member of the RUNX family of transcription factors and has Runt DNA-binding domain. This protein is essential for osteoblastic differentiation and skeletal morphogenesis and acts as a scaffold for nucleic acids and regulatory factors involved in skeletal gene expression. The protein can bind DNA both as a monomer or, with more affinity, as a subunit of a heterodimeric complex. Mutations in this gene have been associated with the bone development disorder cleidocranial dysplasia (CCD). | Cell Differentiation |
| SEPT4 | septin 4 | The protein is a member of the septin family of nucleotide binding proteins, originally described in yeast as cell division cycle regulatory proteins. Septins are highly conserved in yeast, Drosophila, and mouse, and appear to regulate cytoskeletal organization. Disruption of septin function disturbs cytokinesis and results in large multinucleate or polyploid cells. This gene is highly expressed in brain and heart. | Chromosome segregation/kinetochore/spindle/microtubule |
| SMARCA4 | SWI/SNF related, matrix associated, actin dependent regulator of chromatin, | The protein encoded by this gene is a member of the SWI/SNF family of proteins. Members of this family have helicase and ATPase activities and are thought to regulate transcription of certain genes by altering the chromatin structure around those genes. The encoded protein is part of the large ATP-dependent chromatin remodeling complex SNF/SWI, which is required for transcriptional activation of genes normally repressed by chromatin. In addition, this protein can bind BRCA1, as | Chromatin/transcription |

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| | subfamily a, member 4 | well as regulate the expression of the tumorigenic protein CD44. | |
| SMARCB1 | SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily b, member 1 | The protein is part of a complex that relieves repressive chromatin structures, allowing the transcriptional machinery to access its targets more effectively. The encoded nuclear protein may also bind to and enhance the DNA joining activity of HIV-1 integrase. This gene has been found to be a tumor suppressor, and mutations in it have been associated with malignant rhabdoid tumors. | Chromatin/transcription |
| SP3 | Sp3 transcription factor | This gene belongs to a family of Sp1 related genes that encode transcription factors that regulate transcription by binding to consensus GC- and GT-box regulatory elements in target genes. This protein contains a zinc finger DNA-binding domain and several transactivation domains, and has been reported to function as a bifunctional transcription factor that either stimulates or represses the transcription of numerous genes. | Chromatin/transcription |
| SPI1 | spleen focus forming virus (SFFV) proviral integration oncogene spi1 | It is an ETS-domain transcription factor that activates gene expression during myeloid and B-lymphoid cell development. The nuclear protein binds to a purine-rich sequence known as the PU-box found near the promoters of target genes, and regulates their expression in coordination with other transcription factors and cofactors. The protein can also regulate alternative splicing of target genes. | Chromatin/transcription |
| SPIB | Spi-B transcription factor (Spi-1/PU.1 related) | The protein encoded by this gene is a transcriptional activator that binds to the PU-box (5'-GAGGAA-3') and acts as a lymphoid-specific enhancer. | Chromatin/transcription |
| SUV420H1 | suppressor of variegation 4-20 homolog 1 | SUV420H1 (MIM 610881) function as histone methyltransferases that specifically trimethylate nucleosomal histone H4 on lysine-20 (K20). | Chromatin/transcription |
| SUV420H2 | suppressor of variegation 4-20 homolog 2 | SUV420H2 and the related enzyme SUV420H1 (MIM 610881) function as histone methyltransferases that specifically trimethylate nucleosomal histone H4 on lysine-20 (K20). | Chromatin/transcription |
| TFAP2A | transcription factor AP-2 alpha (activating enhancer binding protein 2 alpha) | The protein is a transcription factor that binds the consensus sequence 5'-GCCNNNGGC-3'. The protein functions as either a homodimer or as a heterodimer with similar family members. This protein activates the transcription of some genes while inhibiting the transcription of others. Defects in this gene are a cause of branchiooculofacial syndrome (BOFS). | Cell polarity/morphogenesis |
| TOP2A | topoisomerase (DNA) II alpha 170kDa | It is a DNA topoisomerase, an enzyme that controls and alters the topologic states of DNA during transcription. This nuclear enzyme is involved in processes such as chromosome condensation, chromatid separation, and the relief of torsional stress that occurs during DNA transcription and replication. It catalyzes the transient breaking and rejoining of two strands of duplex DNA which allows the strands to pass through one another, thus altering the topology of DNA. Two forms of this enzyme exist as likely products of a gene duplication event. The gene encoding this form, alpha, is localized to chromosome 17 and the beta gene is localized to chromosome 3. The gene encoding this enzyme functions as the target for several anticancer agents and a variety of mutations in this gene have been associated with the development of drug resistance. Reduced activity of this enzyme may also play a role in ataxia-telangiectasia. | DNA replication/repair/HR/cohesion |
| VHL | von Hippel-Lindau tumor suppressor, E3 ubiquitin | A germline mutation of this gene is the basis of familial inheritance of VHL syndrome. The protein encoded by this gene is a component of the protein complex that includes elongin B, elongin C, and cullin-2, and possesses ubiquitin ligase E3 activity. This protein is involved in the | Protein degradation/proteosome |

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| | protein ligase | ubiquitination and degradation of hypoxia-inducible-factor (HIF), which is a transcription factor that plays a central role in the regulation of gene expression by oxygen. RNA polymerase II subunit POLR2G/RPB7 is also reported to be a target of this protein. | |
| ZBTB16 | zinc finger and BTB domain containing 16 | The protein is a member of the Krueppel C2H2-type zinc-finger protein family and encodes a zinc finger transcription factor that contains nine Kruppel-type zinc finger domains at the carboxyl terminus. This protein is located in the nucleus, is involved in cell cycle progression, and interacts with a histone deacetylase. Specific instances of aberrant gene rearrangement at this locus have been associated with acute promyelocytic leukemia (APL). | Protein degradation/ proteosome |

Table S13. GO term enrichment of Rb interactors**Biological Process**

| GO id | GO name | adjusted-P |
|------------|---|------------|
| GO:0060255 | regulation of macromolecule metabolic process | 6.99E-96 |
| GO:0019222 | regulation of metabolic process | 4.86E-93 |
| GO:0080090 | regulation of primary metabolic process | 1.27E-89 |
| GO:0006351 | transcription, DNA-dependent | 6.96E-89 |
| GO:0031323 | regulation of cellular metabolic process | 8.67E-89 |
| GO:0032774 | RNA biosynthetic process | 7.72E-88 |
| GO:2000112 | regulation of cellular macromolecule biosynthetic process | 3.47E-87 |
| GO:0010468 | regulation of gene expression | 7.26E-87 |
| GO:0006355 | regulation of transcription, DNA-dependent | 2.53E-86 |
| GO:0010556 | regulation of macromolecule biosynthetic process | 3.68E-86 |
| GO:0010467 | gene expression | 8.68E-85 |
| GO:0051252 | regulation of RNA metabolic process | 8.95E-85 |
| GO:0044260 | cellular macromolecule metabolic process | 1.09E-84 |
| GO:0031326 | regulation of cellular biosynthetic process | 1.60E-84 |
| GO:0009889 | regulation of biosynthetic process | 4.75E-84 |
| GO:0043170 | macromolecule metabolic process | 1.80E-82 |
| GO:0051171 | regulation of nitrogen compound metabolic process | 2.46E-82 |
| GO:0034645 | cellular macromolecule biosynthetic process | 2.47E-81 |
| GO:0016070 | RNA metabolic process | 4.74E-81 |
| GO:0019219 | regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 7.55E-81 |
| GO:0009059 | macromolecule biosynthetic process | 5.39E-80 |
| GO:0090304 | nucleic acid metabolic process | 1.32E-78 |
| GO:0006366 | transcription from RNA polymerase II promoter | 6.17E-78 |
| GO:0006139 | nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 1.72E-72 |
| GO:0050794 | regulation of cellular process | 2.19E-72 |
| GO:0048523 | negative regulation of cellular process | 8.10E-71 |
| GO:0050789 | regulation of biological process | 8.48E-69 |
| GO:0044249 | cellular biosynthetic process | 9.14E-69 |
| GO:0006357 | regulation of transcription from RNA polymerase II promoter | 2.34E-68 |
| GO:0044238 | primary metabolic process | 5.00E-68 |
| GO:0007049 | cell cycle | 2.56E-67 |
| GO:0009058 | biosynthetic process | 6.33E-67 |
| GO:0034641 | cellular nitrogen compound metabolic process | 1.98E-66 |
| GO:0048522 | positive regulation of cellular process | 2.84E-66 |
| GO:0048519 | negative regulation of biological process | 1.07E-65 |
| GO:0044237 | cellular metabolic process | 1.41E-65 |
| GO:0010604 | positive regulation of macromolecule metabolic process | 1.05E-64 |
| GO:0006807 | nitrogen compound metabolic process | 1.72E-64 |
| GO:0065007 | biological regulation | 2.13E-64 |
| GO:0031325 | positive regulation of cellular metabolic process | 2.45E-63 |
| GO:0009893 | positive regulation of metabolic process | 4.28E-63 |
| GO:0010605 | negative regulation of macromolecule metabolic process | 7.54E-63 |
| GO:0008152 | metabolic process | 1.78E-62 |
| GO:0009892 | negative regulation of metabolic process | 8.31E-61 |
| GO:0048518 | positive regulation of biological process | 1.09E-60 |
| GO:0031324 | negative regulation of cellular metabolic process | 4.04E-60 |
| GO:0051726 | regulation of cell cycle | 2.68E-59 |
| GO:0010558 | negative regulation of macromolecule biosynthetic process | 2.78E-57 |
| GO:2000113 | negative regulation of cellular macromolecule biosynthetic process | 6.01E-57 |
| GO:0009890 | negative regulation of biosynthetic process | 6.51E-57 |

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| GO:0010629 | negative regulation of gene expression | 1.09E-56 |
| GO:0010628 | positive regulation of gene expression | 1.09E-56 |
| GO:0045892 | negative regulation of transcription, DNA-dependent | 3.22E-56 |
| GO:0031327 | negative regulation of cellular biosynthetic process | 4.15E-56 |
| GO:0051253 | negative regulation of RNA metabolic process | 5.70E-55 |
| GO:0045934 | negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 4.55E-54 |
| GO:0051172 | negative regulation of nitrogen compound metabolic process | 8.89E-54 |
| GO:0045893 | positive regulation of transcription, DNA-dependent | 4.68E-53 |
| GO:0051254 | positive regulation of RNA metabolic process | 5.60E-52 |
| GO:0045935 | positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 6.39E-52 |
| GO:0010557 | positive regulation of macromolecule biosynthetic process | 8.71E-52 |
| GO:0000278 | mitotic cell cycle | 1.22E-51 |
| GO:0051173 | positive regulation of nitrogen compound metabolic process | 2.38E-51 |
| GO:0031328 | positive regulation of cellular biosynthetic process | 9.40E-50 |
| GO:0009891 | positive regulation of biosynthetic process | 2.50E-49 |
| GO:0051276 | chromosome organization | 4.93E-48 |
| GO:0016568 | chromatin modification | 1.46E-47 |
| GO:0022402 | cell cycle process | 3.58E-46 |
| GO:0006325 | chromatin organization | 3.28E-45 |
| GO:0008283 | cell proliferation | 1.34E-44 |
| GO:0043412 | macromolecule modification | 2.02E-43 |
| GO:0051329 | interphase of mitotic cell cycle | 2.13E-43 |
| GO:0045944 | positive regulation of transcription from RNA polymerase II promoter | 2.53E-43 |
| GO:0006464 | protein modification process | 3.03E-43 |
| GO:0051325 | interphase | 4.68E-43 |
| GO:0009987 | cellular process | 5.90E-40 |
| GO:0000122 | negative regulation of transcription from RNA polymerase II promoter | 3.14E-39 |
| GO:0006996 | organelle organization | 5.93E-39 |
| GO:0022403 | cell cycle phase | 8.75E-39 |
| GO:0033554 | cellular response to stress | 8.93E-38 |
| GO:0045786 | negative regulation of cell cycle | 9.74E-38 |
| GO:0071840 | cellular component organization or biogenesis | 2.25E-37 |
| GO:0016043 | cellular component organization | 9.38E-37 |
| GO:0006950 | response to stress | 1.82E-36 |
| GO:0051716 | cellular response to stimulus | 9.30E-36 |
| GO:0042981 | regulation of apoptosis | 1.22E-35 |
| GO:0044267 | cellular protein metabolic process | 1.42E-35 |
| GO:0043067 | regulation of programmed cell death | 2.43E-35 |
| GO:0006915 | apoptosis | 2.84E-35 |
| GO:0012501 | programmed cell death | 6.98E-35 |
| GO:0010941 | regulation of cell death | 1.71E-34 |
| GO:0019538 | protein metabolic process | 6.31E-34 |
| GO:0032502 | developmental process | 1.80E-33 |
| GO:0016569 | covalent chromatin modification | 2.03E-33 |
| GO:0007050 | cell cycle arrest | 2.33E-33 |
| GO:0008219 | cell death | 2.93E-33 |
| GO:0016265 | death | 3.09E-33 |
| GO:0065009 | regulation of molecular function | 6.39E-33 |
| GO:0006974 | response to DNA damage stimulus | 1.06E-32 |
| GO:0042127 | regulation of cell proliferation | 2.44E-32 |
| GO:0016570 | histone modification | 2.93E-32 |
| GO:0010564 | regulation of cell cycle process | 7.08E-32 |
| GO:0071841 | cellular component organization or biogenesis at cellular level | 2.27E-31 |
| GO:0050896 | response to stimulus | 5.10E-31 |
| GO:0071842 | cellular component organization at cellular level | 1.05E-30 |
| GO:0008150 | biological_process | 1.21E-30 |
| GO:0071156 | regulation of cell cycle arrest | 5.42E-30 |

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| GO:0051246 | regulation of protein metabolic process | 5.86E-30 |
| GO:0032501 | multicellular organismal process | 1.74E-29 |
| GO:0022414 | reproductive process | 1.14E-28 |
| GO:0022415 | viral reproductive process | 1.32E-28 |
| GO:0000003 | reproduction | 1.37E-28 |
| GO:0007275 | multicellular organismal development | 5.20E-28 |
| GO:0048513 | organ development | 1.39E-27 |
| GO:0000082 | G1/S transition of mitotic cell cycle | 2.80E-27 |
| GO:0044403 | symbiosis, encompassing mutualism through parasitism | 3.80E-27 |
| GO:0044419 | interspecies interaction between organisms | 3.80E-27 |
| GO:0048856 | anatomical structure development | 5.93E-27 |
| GO:0032268 | regulation of cellular protein metabolic process | 7.91E-27 |
| GO:0031399 | regulation of protein modification process | 3.14E-26 |
| GO:0045595 | regulation of cell differentiation | 3.54E-26 |
| GO:0016032 | viral reproduction | 5.07E-26 |
| GO:0019048 | virus-host interaction | 9.99E-26 |
| GO:0030154 | cell differentiation | 1.02E-25 |
| GO:0048731 | system development | 1.26E-25 |
| GO:0007346 | regulation of mitotic cell cycle | 1.31E-25 |
| GO:0050793 | regulation of developmental process | 4.85E-25 |
| GO:0006259 | DNA metabolic process | 8.67E-25 |
| GO:0000080 | G1 phase of mitotic cell cycle | 9.35E-25 |
| GO:0051318 | G1 phase | 2.20E-24 |
| GO:0050790 | regulation of catalytic activity | 4.85E-24 |
| GO:0048869 | cellular developmental process | 5.24E-24 |
| GO:0042221 | response to chemical stimulus | 5.43E-24 |
| GO:0051094 | positive regulation of developmental process | 5.78E-24 |
| GO:0051701 | interaction with host | 1.31E-23 |
| GO:0006367 | transcription initiation from RNA polymerase II promoter | 2.26E-23 |
| GO:0000075 | cell cycle checkpoint | 3.71E-23 |
| GO:0006352 | transcription initiation, DNA-dependent | 6.34E-23 |
| GO:0044093 | positive regulation of molecular function | 1.21E-22 |
| GO:0051704 | multi-organism process | 4.93E-22 |
| GO:0000077 | DNA damage checkpoint | 1.35E-21 |
| GO:0031570 | DNA integrity checkpoint | 3.71E-21 |
| GO:0051301 | cell division | 4.91E-21 |
| GO:0007167 | enzyme linked receptor protein signaling pathway | 4.92E-21 |
| GO:0010033 | response to organic substance | 5.09E-21 |
| GO:0065008 | regulation of biological quality | 5.63E-21 |
| GO:0006793 | phosphorus metabolic process | 5.88E-21 |
| GO:0006796 | phosphate metabolic process | 5.88E-21 |
| GO:0030099 | myeloid cell differentiation | 8.39E-21 |
| GO:0016310 | phosphorylation | 1.17E-20 |
| GO:0007165 | signal transduction | 1.20E-20 |
| GO:0070887 | cellular response to chemical stimulus | 2.57E-20 |
| GO:0023052 | signaling | 8.12E-20 |
| GO:0006468 | protein phosphorylation | 1.10E-19 |
| GO:0043068 | positive regulation of programmed cell death | 2.27E-19 |
| GO:0010942 | positive regulation of cell death | 5.25E-19 |
| GO:0051239 | regulation of multicellular organismal process | 1.53E-18 |
| GO:0042770 | signal transduction in response to DNA damage | 1.67E-18 |
| GO:0043065 | positive regulation of apoptosis | 1.87E-18 |
| GO:2000602 | regulation of interphase of mitotic cell cycle | 1.87E-18 |
| GO:2000026 | regulation of multicellular organismal development | 2.63E-18 |
| GO:0007093 | mitotic cell cycle checkpoint | 1.13E-17 |
| GO:0043066 | negative regulation of apoptosis | 1.33E-17 |
| GO:0043069 | negative regulation of programmed cell death | 2.05E-17 |
| GO:0032270 | positive regulation of cellular protein metabolic process | 2.23E-17 |
| GO:0043085 | positive regulation of catalytic activity | 2.98E-17 |

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| GO:0045597 | positive regulation of cell differentiation | 4.02E-17 |
| GO:0008284 | positive regulation of cell proliferation | 4.32E-17 |
| GO:0045637 | regulation of myeloid cell differentiation | 5.02E-17 |
| GO:0007166 | cell surface receptor linked signaling pathway | 8.13E-17 |
| GO:0060548 | negative regulation of cell death | 9.29E-17 |
| GO:0051247 | positive regulation of protein metabolic process | 1.25E-16 |
| GO:0030330 | DNA damage response, signal transduction by p53 class mediator | 4.34E-16 |
| GO:0032446 | protein modification by small protein conjugation | 5.89E-16 |
| GO:0048583 | regulation of response to stimulus | 5.91E-16 |
| GO:0072331 | signal transduction by p53 class mediator | 8.16E-16 |
| GO:0009653 | anatomical structure morphogenesis | 8.30E-16 |
| GO:0007569 | cell aging | 8.39E-16 |
| GO:0007179 | transforming growth factor beta receptor signaling pathway | 8.62E-16 |
| GO:0051128 | regulation of cellular component organization | 1.17E-15 |
| GO:0031401 | positive regulation of protein modification process | 1.97E-15 |
| GO:0002376 | immune system process | 2.27E-15 |
| GO:0030097 | hemopoiesis | 2.42E-15 |
| GO:0009790 | embryo development | 4.98E-15 |
| GO:0002682 | regulation of immune system process | 7.07E-15 |
| GO:0070647 | protein modification by small protein conjugation or removal | 9.72E-15 |
| GO:0006260 | DNA replication | 9.94E-15 |
| GO:0008285 | negative regulation of cell proliferation | 1.09E-14 |
| GO:0048534 | hemopoietic or lymphoid organ development | 1.28E-14 |
| GO:0016567 | protein ubiquitination | 1.38E-14 |
| GO:0042325 | regulation of phosphorylation | 1.56E-14 |
| GO:0051338 | regulation of transferase activity | 1.68E-14 |
| GO:0009719 | response to endogenous stimulus | 1.79E-14 |
| GO:0018205 | peptidyl-lysine modification | 1.87E-14 |
| GO:2000045 | regulation of G1/S transition of mitotic cell cycle | 1.91E-14 |
| GO:0051320 | S phase | 2.29E-14 |
| GO:0009314 | response to radiation | 7.04E-14 |
| GO:0048585 | negative regulation of response to stimulus | 7.97E-14 |
| GO:0002520 | immune system development | 8.56E-14 |
| GO:0044092 | negative regulation of molecular function | 1.08E-13 |
| GO:0051248 | negative regulation of protein metabolic process | 1.25E-13 |
| GO:0000084 | S phase of mitotic cell cycle | 1.33E-13 |
| GO:0045646 | regulation of erythrocyte differentiation | 2.21E-13 |
| GO:0007178 | transmembrane receptor protein serine/threonine kinase signaling pathway | 2.46E-13 |
| GO:0019220 | regulation of phosphate metabolic process | 2.54E-13 |
| GO:0051174 | regulation of phosphorus metabolic process | 2.54E-13 |
| GO:0031400 | negative regulation of protein modification process | 3.99E-13 |
| GO:0043549 | regulation of kinase activity | 6.00E-13 |
| GO:0032269 | negative regulation of cellular protein metabolic process | 8.29E-13 |
| GO:0071158 | positive regulation of cell cycle arrest | 8.41E-13 |
| GO:0009966 | regulation of signal transduction | 9.56E-13 |
| GO:0006281 | DNA repair | 1.16E-12 |
| GO:0009725 | response to hormone stimulus | 1.72E-12 |
| GO:0009628 | response to abiotic stimulus | 1.89E-12 |
| GO:0080134 | regulation of response to stress | 2.64E-12 |
| GO:0033044 | regulation of chromosome organization | 2.97E-12 |
| GO:0018193 | peptidyl-amino acid modification | 2.98E-12 |
| GO:0071310 | cellular response to organic substance | 5.82E-12 |
| GO:0009968 | negative regulation of signal transduction | 6.15E-12 |
| GO:0002573 | myeloid leukocyte differentiation | 6.54E-12 |
| GO:0030522 | intracellular receptor mediated signaling pathway | 7.54E-12 |
| GO:0010646 | regulation of cell communication | 8.20E-12 |
| GO:0001932 | regulation of protein phosphorylation | 9.39E-12 |
| GO:0023051 | regulation of signaling | 9.76E-12 |
| GO:0051090 | regulation of sequence-specific DNA binding transcription factor activity | 1.01E-11 |

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| GO:0031056 | regulation of histone modification | 1.16E-11 |
| GO:0031571 | mitotic cell cycle G1/S transition DNA damage checkpoint | 1.16E-11 |
| GO:0007568 | aging | 1.22E-11 |
| GO:0006917 | induction of apoptosis | 1.63E-11 |
| GO:0012502 | induction of programmed cell death | 2.06E-11 |
| GO:0023057 | negative regulation of signaling | 3.39E-11 |
| GO:0007154 | cell communication | 3.79E-11 |
| GO:0010648 | negative regulation of cell communication | 3.88E-11 |
| GO:0090068 | positive regulation of cell cycle process | 6.15E-11 |
| GO:0031575 | mitotic cell cycle G1/S transition checkpoint | 6.64E-11 |
| GO:0071779 | G1/S transition checkpoint | 8.66E-11 |
| GO:0000086 | G2/M transition of mitotic cell cycle | 1.02E-10 |
| GO:0045859 | regulation of protein kinase activity | 1.24E-10 |
| GO:0000079 | regulation of cyclin-dependent protein kinase activity | 1.46E-10 |
| GO:0040008 | regulation of growth | 1.49E-10 |
| GO:0009611 | response to wounding | 2.25E-10 |
| GO:0000083 | regulation of transcription involved in G1/S phase of mitotic cell cycle | 3.10E-10 |
| GO:0009411 | response to UV | 4.29E-10 |
| GO:0030218 | erythrocyte differentiation | 4.29E-10 |
| GO:0035556 | intracellular signal transduction | 5.51E-10 |
| GO:0033043 | regulation of organelle organization | 5.64E-10 |
| GO:0007399 | nervous system development | 5.85E-10 |
| GO:0006383 | transcription from RNA polymerase III promoter | 6.76E-10 |
| GO:0048468 | cell development | 7.67E-10 |
| GO:0034101 | erythrocyte homeostasis | 8.86E-10 |
| GO:0009057 | macromolecule catabolic process | 9.77E-10 |
| GO:0009416 | response to light stimulus | 1.12E-09 |
| GO:0051129 | negative regulation of cellular component organization | 1.45E-09 |
| GO:0002521 | leukocyte differentiation | 1.45E-09 |
| GO:0043086 | negative regulation of catalytic activity | 1.51E-09 |
| GO:0071478 | cellular response to radiation | 1.74E-09 |
| GO:0043525 | positive regulation of neuron apoptosis | 1.88E-09 |
| GO:0051052 | regulation of DNA metabolic process | 1.93E-09 |
| GO:0090398 | cellular senescence | 2.27E-09 |
| GO:0009887 | organ morphogenesis | 2.32E-09 |
| GO:0031145 | anaphase-promoting complex-dependent proteasomal ubiquitin-dependent protein catabolic process | 2.83E-09 |
| GO:0051093 | negative regulation of developmental process | 3.07E-09 |
| GO:0072401 | signal transduction involved in DNA integrity checkpoint | 4.71E-09 |
| GO:0072422 | signal transduction involved in DNA damage checkpoint | 4.71E-09 |
| GO:0018394 | peptidyl-lysine acetylation | 4.91E-09 |
| GO:0031396 | regulation of protein ubiquitination | 5.10E-09 |
| GO:0043414 | macromolecule methylation | 5.10E-09 |
| GO:0006338 | chromatin remodeling | 5.38E-09 |
| GO:0072395 | signal transduction involved in cell cycle checkpoint | 5.45E-09 |
| GO:0006730 | one-carbon metabolic process | 5.63E-09 |
| GO:0071495 | cellular response to endogenous stimulus | 8.01E-09 |
| GO:0045639 | positive regulation of myeloid cell differentiation | 8.31E-09 |
| GO:0007169 | transmembrane receptor protein tyrosine kinase signaling pathway | 8.58E-09 |
| GO:0032259 | methylation | 1.02E-08 |
| GO:0040007 | growth | 1.07E-08 |
| GO:0043921 | modulation by host of viral transcription | 1.10E-08 |
| GO:0052472 | modulation by host of symbiont transcription | 1.10E-08 |
| GO:0000280 | nuclear division | 1.34E-08 |
| GO:0007067 | mitosis | 1.34E-08 |
| GO:0071214 | cellular response to abiotic stimulus | 1.46E-08 |
| GO:0050792 | regulation of viral reproduction | 1.47E-08 |
| GO:0007423 | sensory organ development | 1.50E-08 |
| GO:0048524 | positive regulation of viral reproduction | 1.61E-08 |

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| GO:0071453 | cellular response to oxygen levels | 1.61E-08 |
| GO:0090342 | regulation of cell aging | 1.63E-08 |
| GO:0044265 | cellular macromolecule catabolic process | 1.67E-08 |
| GO:0006473 | protein acetylation | 2.10E-08 |
| GO:0048872 | homeostasis of number of cells | 2.14E-08 |
| GO:0052312 | modulation of transcription in other organism involved in symbiotic interaction | 2.38E-08 |
| GO:0044257 | cellular protein catabolic process | 2.54E-08 |
| GO:0000087 | M phase of mitotic cell cycle | 2.58E-08 |
| GO:0030163 | protein catabolic process | 2.71E-08 |
| GO:0043161 | proteasomal ubiquitin-dependent protein catabolic process | 3.02E-08 |
| GO:0072358 | cardiovascular system development | 3.21E-08 |
| GO:0072359 | circulatory system development | 3.21E-08 |
| GO:0048011 | nerve growth factor receptor signaling pathway | 3.63E-08 |
| GO:0001654 | eye development | 3.67E-08 |
| GO:0048545 | response to steroid hormone stimulus | 3.85E-08 |
| GO:0010035 | response to inorganic substance | 4.06E-08 |
| GO:0048285 | organelle fission | 4.36E-08 |
| GO:0010498 | proteasomal protein catabolic process | 4.65E-08 |
| GO:0030518 | steroid hormone receptor signaling pathway | 5.08E-08 |
| GO:0060284 | regulation of cell development | 5.23E-08 |
| GO:0016573 | histone acetylation | 6.07E-08 |
| GO:0045648 | positive regulation of erythrocyte differentiation | 6.61E-08 |
| GO:0008361 | regulation of cell size | 8.33E-08 |
| GO:0018393 | internal peptidyl-lysine acetylation | 8.59E-08 |
| GO:0042592 | homeostatic process | 8.76E-08 |
| GO:0071900 | regulation of protein serine/threonine kinase activity | 8.83E-08 |
| GO:0010639 | negative regulation of organelle organization | 9.27E-08 |
| GO:0030521 | androgen receptor signaling pathway | 9.88E-08 |
| GO:0051603 | proteolysis involved in cellular protein catabolic process | 1.20E-07 |
| GO:0051851 | modification by host of symbiont morphology or physiology | 1.21E-07 |
| GO:0010212 | response to ionizing radiation | 1.22E-07 |
| GO:0046782 | regulation of viral transcription | 1.30E-07 |
| GO:0006475 | internal protein amino acid acetylation | 1.41E-07 |
| GO:0006977 | DNA damage response, signal transduction by p53 class mediator resulting in cell cycle arrest | 1.48E-07 |
| GO:0072413 | signal transduction involved in mitotic cell cycle checkpoint | 1.48E-07 |
| GO:0072431 | signal transduction involved in mitotic cell cycle G1/S transition DNA damage checkpoint | 1.48E-07 |
| GO:0072474 | signal transduction involved in mitotic cell cycle G1/S checkpoint | 1.48E-07 |
| GO:0072404 | signal transduction involved in G1/S transition checkpoint | 1.69E-07 |
| GO:0031397 | negative regulation of protein ubiquitination | 1.71E-07 |
| GO:0043523 | regulation of neuron apoptosis | 1.74E-07 |
| GO:0048568 | embryonic organ development | 1.89E-07 |
| GO:0006511 | ubiquitin-dependent protein catabolic process | 1.91E-07 |
| GO:0006476 | protein deacetylation | 1.92E-07 |
| GO:0009888 | tissue development | 2.06E-07 |
| GO:0010038 | response to metal ion | 2.28E-07 |
| GO:0019941 | modification-dependent protein catabolic process | 2.29E-07 |
| GO:0043543 | protein acylation | 2.35E-07 |
| GO:0071456 | cellular response to hypoxia | 2.47E-07 |
| GO:0043632 | modification-dependent macromolecule catabolic process | 2.48E-07 |
| GO:0035601 | protein deacylation | 2.79E-07 |
| GO:0000279 | M phase | 3.04E-07 |
| GO:0016575 | histone deacetylation | 3.50E-07 |
| GO:0051439 | regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle | 4.00E-07 |
| GO:0031576 | G2/M transition checkpoint | 4.12E-07 |
| GO:0051702 | interaction with symbiont | 4.45E-07 |
| GO:0043010 | camera-type eye development | 5.21E-07 |
| GO:2000241 | regulation of reproductive process | 5.22E-07 |

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| GO:0019058 | viral infectious cycle | 5.83E-07 |
| GO:0051402 | neuron apoptosis | 5.83E-07 |
| GO:0032870 | cellular response to hormone stimulus | 6.37E-07 |
| GO:0032535 | regulation of cellular component size | 6.41E-07 |
| GO:0044248 | cellular catabolic process | 6.91E-07 |
| GO:0070997 | neuron death | 7.11E-07 |
| GO:0007243 | intracellular protein kinase cascade | 7.40E-07 |
| GO:0016571 | histone methylation | 9.74E-07 |
| GO:0045596 | negative regulation of cell differentiation | 1.05E-06 |
| GO:0008629 | induction of apoptosis by intracellular signals | 1.08E-06 |
| GO:0034968 | histone lysine methylation | 1.17E-06 |
| GO:0050878 | regulation of body fluid levels | 1.30E-06 |
| GO:0031057 | negative regulation of histone modification | 1.66E-06 |
| GO:0090066 | regulation of anatomical structure size | 1.89E-06 |
| GO:0016049 | cell growth | 2.15E-06 |
| GO:0008630 | DNA damage response, signal transduction resulting in induction of apoptosis | 2.30E-06 |
| GO:0043281 | regulation of caspase activity | 2.31E-06 |
| GO:0048646 | anatomical structure formation involved in morphogenesis | 2.33E-06 |
| GO:0031572 | G2/M transition DNA damage checkpoint | 2.38E-06 |
| GO:0043280 | positive regulation of caspase activity | 2.42E-06 |
| GO:0080135 | regulation of cellular response to stress | 2.74E-06 |
| GO:0010001 | glial cell differentiation | 2.96E-06 |
| GO:0006479 | protein methylation | 3.02E-06 |
| GO:0008213 | protein alkylation | 3.02E-06 |
| GO:0043923 | positive regulation by host of viral transcription | 3.24E-06 |
| GO:0006461 | protein complex assembly | 3.63E-06 |
| GO:0048699 | generation of neurons | 3.68E-06 |
| GO:0010948 | negative regulation of cell cycle process | 3.74E-06 |
| GO:0070271 | protein complex biogenesis | 3.76E-06 |
| GO:0010952 | positive regulation of peptidase activity | 4.01E-06 |
| GO:0034644 | cellular response to UV | 4.04E-06 |
| GO:0040029 | regulation of gene expression, epigenetic | 4.42E-06 |
| GO:0051438 | regulation of ubiquitin-protein ligase activity | 4.51E-06 |
| GO:0007417 | central nervous system development | 4.59E-06 |
| GO:0035821 | modification of morphology or physiology of other organism | 4.75E-06 |
| GO:0051817 | modification of morphology or physiology of other organism involved in symbiotic interaction | 4.75E-06 |
| GO:2000243 | positive regulation of reproductive process | 4.92E-06 |
| GO:0052548 | regulation of endopeptidase activity | 5.09E-06 |
| GO:0045787 | positive regulation of cell cycle | 5.27E-06 |
| GO:0048598 | embryonic morphogenesis | 5.30E-06 |
| GO:0032504 | multicellular organism reproduction | 5.39E-06 |
| GO:0048609 | multicellular organismal reproductive process | 5.39E-06 |
| GO:0044085 | cellular component biogenesis | 5.93E-06 |
| GO:0051437 | positive regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle | 5.96E-06 |
| GO:0043009 | chordate embryonic development | 6.31E-06 |
| GO:0051340 | regulation of ligase activity | 6.34E-06 |
| GO:0052547 | regulation of peptidase activity | 7.01E-06 |
| GO:0006302 | double-strand break repair | 8.37E-06 |
| GO:0009792 | embryo development ending in birth or egg hatching | 8.41E-06 |
| GO:0042060 | wound healing | 8.67E-06 |
| GO:0006508 | proteolysis | 8.72E-06 |
| GO:0045165 | cell fate commitment | 8.97E-06 |
| GO:0001775 | cell activation | 8.98E-06 |
| GO:0071482 | cellular response to light stimulus | 8.98E-06 |
| GO:0051403 | stress-activated MAPK cascade | 9.20E-06 |
| GO:0007596 | blood coagulation | 9.28E-06 |
| GO:0031398 | positive regulation of protein ubiquitination | 1.01E-05 |

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| GO:0071496 | cellular response to external stimulus | 1.03E-05 |
| GO:0007599 | hemostasis | 1.08E-05 |
| GO:0051130 | positive regulation of cellular component organization | 1.18E-05 |
| GO:0033143 | regulation of steroid hormone receptor signaling pathway | 1.21E-05 |
| GO:0042063 | gliogenesis | 1.25E-05 |
| GO:0006978 | DNA damage response, signal transduction by p53 class mediator resulting in transcription of p21 class mediator | 1.37E-05 |
| GO:0050817 | coagulation | 1.38E-05 |
| GO:0051960 | regulation of nervous system development | 1.58E-05 |
| GO:0051443 | positive regulation of ubiquitin-protein ligase activity | 1.87E-05 |
| GO:0007507 | heart development | 1.98E-05 |
| GO:0042772 | DNA damage response, signal transduction resulting in transcription | 2.04E-05 |
| GO:0032844 | regulation of homeostatic process | 2.17E-05 |
| GO:0022008 | neurogenesis | 2.21E-05 |
| GO:0051573 | negative regulation of histone H3-K9 methylation | 2.32E-05 |
| GO:0043933 | macromolecular complex subunit organization | 2.37E-05 |
| GO:0050767 | regulation of neurogenesis | 2.44E-05 |
| GO:0051101 | regulation of DNA binding | 2.71E-05 |
| GO:0051351 | positive regulation of ligase activity | 2.71E-05 |
| GO:0050434 | positive regulation of viral transcription | 2.72E-05 |
| GO:0030219 | megakaryocyte differentiation | 3.17E-05 |
| GO:0065003 | macromolecular complex assembly | 3.17E-05 |
| GO:0048584 | positive regulation of response to stimulus | 3.53E-05 |
| GO:0071822 | protein complex subunit organization | 3.77E-05 |
| GO:0031331 | positive regulation of cellular catabolic process | 4.09E-05 |
| GO:0001558 | regulation of cell growth | 4.14E-05 |
| GO:0006913 | nucleocytoplasmic transport | 4.16E-05 |
| GO:0051169 | nuclear transport | 4.51E-05 |
| GO:0030225 | macrophage differentiation | 4.60E-05 |
| GO:2000756 | regulation of peptidyl-lysine acetylation | 4.60E-05 |
| GO:0048145 | regulation of fibroblast proliferation | 4.60E-05 |
| GO:0009056 | catabolic process | 5.40E-05 |
| GO:0009896 | positive regulation of catabolic process | 5.60E-05 |
| GO:0048144 | fibroblast proliferation | 5.91E-05 |
| GO:0009605 | response to external stimulus | 6.00E-05 |
| GO:0043627 | response to estrogen stimulus | 6.61E-05 |
| GO:0006261 | DNA-dependent DNA replication | 6.84E-05 |
| GO:0006310 | DNA recombination | 7.11E-05 |
| GO:0034599 | cellular response to oxidative stress | 7.27E-05 |
| GO:0007420 | brain development | 8.20E-05 |
| GO:0035666 | TRIF-dependent toll-like receptor signaling pathway | 9.71E-05 |
| GO:0051436 | negative regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle | 9.71E-05 |
| GO:0048610 | cellular process involved in reproduction | 1.05E-04 |
| GO:0043470 | regulation of carbohydrate catabolic process | 1.06E-04 |
| GO:0043471 | regulation of cellular carbohydrate catabolic process | 1.06E-04 |
| GO:0045814 | negative regulation of gene expression, epigenetic | 1.06E-04 |
| GO:0022607 | cellular component assembly | 1.32E-04 |
| GO:0071897 | DNA biosynthetic process | 1.44E-04 |
| GO:0042493 | response to drug | 1.54E-04 |
| GO:0001701 | in utero embryonic development | 1.54E-04 |
| GO:0019080 | viral genome expression | 1.56E-04 |
| GO:0019083 | viral transcription | 1.56E-04 |
| GO:0002756 | MyD88-independent toll-like receptor signaling pathway | 1.61E-04 |
| GO:0034138 | toll-like receptor 3 signaling pathway | 1.77E-04 |
| GO:0009894 | regulation of catabolic process | 1.87E-04 |
| GO:0090343 | positive regulation of cell aging | 1.90E-04 |
| GO:0090344 | negative regulation of cell aging | 1.90E-04 |
| GO:0060765 | regulation of androgen receptor signaling pathway | 2.19E-04 |

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| GO:0050673 | epithelial cell proliferation | 2.19E-04 |
| GO:0048592 | eye morphogenesis | 2.33E-04 |
| GO:0031058 | positive regulation of histone modification | 2.51E-04 |
| GO:0051352 | negative regulation of ligase activity | 2.56E-04 |
| GO:0051444 | negative regulation of ubiquitin-protein ligase activity | 2.56E-04 |
| GO:0042327 | positive regulation of phosphorylation | 2.57E-04 |
| GO:0070482 | response to oxygen levels | 2.83E-04 |
| GO:0030512 | negative regulation of transforming growth factor beta receptor signaling pathway | 3.06E-04 |
| GO:0045444 | fat cell differentiation | 3.14E-04 |
| GO:0051570 | regulation of histone H3-K9 methylation | 3.15E-04 |
| GO:2000377 | regulation of reactive oxygen species metabolic process | 3.34E-04 |
| GO:0010562 | positive regulation of phosphorus metabolic process | 3.51E-04 |
| GO:0045937 | positive regulation of phosphate metabolic process | 3.51E-04 |
| GO:0051348 | negative regulation of transferase activity | 3.71E-04 |
| GO:0006921 | cellular component disassembly involved in apoptosis | 3.96E-04 |
| GO:0008063 | Toll signaling pathway | 3.96E-04 |
| GO:0043966 | histone H3 acetylation | 4.18E-04 |
| GO:0031061 | negative regulation of histone methylation | 4.92E-04 |
| GO:0010608 | posttranscriptional regulation of gene expression | 4.97E-04 |
| GO:0017015 | regulation of transforming growth factor beta receptor signaling pathway | 5.21E-04 |
| GO:0071241 | cellular response to inorganic substance | 5.21E-04 |
| GO:0030855 | epithelial cell differentiation | 5.52E-04 |
| GO:0051384 | response to glucocorticoid stimulus | 5.77E-04 |
| GO:0006354 | transcription elongation, DNA-dependent | 5.87E-04 |
| GO:0045321 | leukocyte activation | 6.10E-04 |
| GO:0032869 | cellular response to insulin stimulus | 6.82E-04 |
| GO:0051336 | regulation of hydrolase activity | 7.23E-04 |
| GO:0031060 | regulation of histone methylation | 7.47E-04 |
| GO:0031960 | response to corticosteroid stimulus | 8.14E-04 |
| GO:0030278 | regulation of ossification | 8.45E-04 |
| GO:0001890 | placenta development | 8.57E-04 |
| GO:0034142 | toll-like receptor 4 signaling pathway | 8.72E-04 |
| GO:0042771 | DNA damage response, signal transduction by p53 class mediator resulting in induction of apoptosis | 8.92E-04 |
| GO:0043516 | regulation of DNA damage response, signal transduction by p53 class mediator | 8.92E-04 |
| GO:0048146 | positive regulation of fibroblast proliferation | 9.23E-04 |
| GO:0032879 | regulation of localization | 9.38E-04 |
| GO:0030308 | negative regulation of cell growth | 9.79E-04 |
| GO:0002757 | immune response-activating signal transduction | 0.001062 |
| GO:0051054 | positive regulation of DNA metabolic process | 0.001094 |
| GO:0000209 | protein polyubiquitination | 0.001115 |
| GO:0001934 | positive regulation of protein phosphorylation | 0.001129 |
| GO:0006275 | regulation of DNA replication | 0.001218 |
| GO:0010720 | positive regulation of cell development | 0.001259 |
| GO:0007283 | spermatogenesis | 0.001287 |
| GO:0048232 | male gamete generation | 0.001315 |
| GO:0032070 | regulation of deoxyribonuclease activity | 0.001326 |
| GO:0031668 | cellular response to extracellular stimulus | 0.001399 |
| GO:0002764 | immune response-regulating signaling pathway | 0.001439 |
| GO:0006979 | response to oxidative stress | 0.00144 |
| GO:0043518 | negative regulation of DNA damage response, signal transduction by p53 class mediator | 0.001457 |
| GO:0060766 | negative regulation of androgen receptor signaling pathway | 0.001457 |
| GO:0035065 | regulation of histone acetylation | 0.001458 |
| GO:0051345 | positive regulation of hydrolase activity | 0.001489 |
| GO:0071375 | cellular response to peptide hormone stimulus | 0.001515 |
| GO:0032868 | response to insulin stimulus | 0.001555 |
| GO:0045088 | regulation of innate immune response | 0.001603 |

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| GO:0045860 | positive regulation of protein kinase activity | 0.001652 |
| GO:0045792 | negative regulation of cell size | 0.001694 |
| GO:0051568 | histone H3-K4 methylation | 0.0017 |
| GO:0010627 | regulation of intracellular protein kinase cascade | 0.001753 |
| GO:0006919 | activation of caspase activity | 0.00187 |
| GO:0051091 | positive regulation of sequence-specific DNA binding transcription factor activity | 0.001913 |
| GO:0002221 | pattern recognition receptor signaling pathway | 0.001932 |
| GO:0005981 | regulation of glycogen catabolic process | 0.00197 |
| GO:0071780 | mitotic cell cycle G2/M transition checkpoint | 0.00197 |
| GO:0090399 | replicative senescence | 0.00197 |
| GO:0010332 | response to gamma radiation | 0.002013 |
| GO:0048708 | astrocyte differentiation | 0.002013 |
| GO:0048863 | stem cell differentiation | 0.002028 |
| GO:0030182 | neuron differentiation | 0.002141 |
| GO:0010906 | regulation of glucose metabolic process | 0.002265 |
| GO:0035162 | embryonic hemopoiesis | 0.002274 |
| GO:0072332 | signal transduction by p53 class mediator resulting in induction of apoptosis | 0.002274 |
| GO:0002758 | innate immune response-activating signal transduction | 0.002464 |
| GO:0034504 | protein localization to nucleus | 0.002624 |
| GO:0034130 | toll-like receptor 1 signaling pathway | 0.002627 |
| GO:0050769 | positive regulation of neurogenesis | 0.002824 |
| GO:0001836 | release of cytochrome c from mitochondria | 0.002865 |
| GO:0002761 | regulation of myeloid leukocyte differentiation | 0.002902 |
| GO:0071248 | cellular response to metal ion | 0.002902 |
| GO:0033674 | positive regulation of kinase activity | 0.002948 |
| GO:0001503 | ossification | 0.002967 |
| GO:0031329 | regulation of cellular catabolic process | 0.003005 |
| GO:0060429 | epithelium development | 0.003064 |
| GO:0034097 | response to cytokine stimulus | 0.003165 |
| GO:0090239 | regulation of histone H4 acetylation | 0.003255 |
| GO:0090101 | negative regulation of transmembrane receptor protein serine/threonine kinase signaling pathway | 0.003271 |
| GO:0045737 | positive regulation of cyclin-dependent protein kinase activity | 0.003381 |
| GO:0051567 | histone H3-K9 methylation | 0.003381 |
| GO:0030851 | granulocyte differentiation | 0.003413 |
| GO:0016458 | gene silencing | 0.003469 |
| GO:0031098 | stress-activated protein kinase signaling cascade | 0.003496 |
| GO:0009607 | response to biotic stimulus | 0.003574 |
| GO:0051347 | positive regulation of transferase activity | 0.003706 |
| GO:0045926 | negative regulation of growth | 0.003716 |
| GO:0048593 | camera-type eye morphogenesis | 0.003732 |
| GO:0050678 | regulation of epithelial cell proliferation | 0.003832 |
| GO:0014013 | regulation of gliogenesis | 0.003894 |
| GO:0048660 | regulation of smooth muscle cell proliferation | 0.003894 |
| GO:0043467 | regulation of generation of precursor metabolites and energy | 0.003975 |
| GO:0002218 | activation of innate immune response | 0.004078 |
| GO:0010869 | regulation of receptor biosynthetic process | 0.004309 |
| GO:0043434 | response to peptide hormone stimulus | 0.004384 |
| GO:0000165 | MAPKKK cascade | 0.004466 |
| GO:0034134 | toll-like receptor 2 signaling pathway | 0.004655 |
| GO:0033002 | muscle cell proliferation | 0.00486 |
| GO:0001892 | embryonic placenta development | 0.004882 |
| GO:0048659 | smooth muscle cell proliferation | 0.004882 |
| GO:0031347 | regulation of defense response | 0.005108 |
| GO:0051569 | regulation of histone H3-K4 methylation | 0.005422 |
| GO:0051149 | positive regulation of muscle cell differentiation | 0.005857 |
| GO:0001889 | liver development | 0.006276 |
| GO:0031647 | regulation of protein stability | 0.006419 |
| GO:0006606 | protein import into nucleus | 0.006525 |

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| GO:0000216 | M/G1 transition of mitotic cell cycle | 0.006783 |
| GO:0002755 | MyD88-dependent toll-like receptor signaling pathway | 0.006783 |
| GO:0061008 | hepaticobiliary system development | 0.006808 |
| GO:0001666 | response to hypoxia | 0.006872 |
| GO:0007219 | Notch signaling pathway | 0.007093 |
| GO:0051170 | nuclear import | 0.007099 |
| GO:0010675 | regulation of cellular carbohydrate metabolic process | 0.007123 |
| GO:0046649 | lymphocyte activation | 0.007341 |
| GO:0006109 | regulation of carbohydrate metabolic process | 0.007505 |
| GO:0009991 | response to extracellular stimulus | 0.007535 |
| GO:0042176 | regulation of protein catabolic process | 0.008108 |
| GO:0006270 | DNA-dependent DNA replication initiation | 0.008694 |
| GO:0043392 | negative regulation of DNA binding | 0.008694 |
| GO:0042113 | B cell activation | 0.008939 |
| GO:0008637 | apoptotic mitochondrial changes | 0.008993 |
| GO:0045638 | negative regulation of myeloid cell differentiation | 0.008993 |
| GO:0030162 | regulation of proteolysis | 0.009533 |
| GO:0019953 | sexual reproduction | 0.009643 |
| GO:0050872 | white fat cell differentiation | 0.010029 |
| GO:0032355 | response to estradiol stimulus | 0.010539 |
| GO:0071479 | cellular response to ionizing radiation | 0.010688 |
| GO:0009304 | tRNA transcription | 0.011088 |
| GO:0010243 | response to organic nitrogen | 0.011157 |
| GO:0035295 | tube development | 0.011235 |
| GO:0043967 | histone H4 acetylation | 0.011814 |
| GO:2000145 | regulation of cell motility | 0.012811 |
| GO:0030900 | forebrain development | 0.012915 |
| GO:0033365 | protein localization to organelle | 0.013 |
| GO:0006282 | regulation of DNA repair | 0.013033 |
| GO:0045089 | positive regulation of innate immune response | 0.014236 |
| GO:0035019 | somatic stem cell maintenance | 0.014357 |
| GO:0032800 | receptor biosynthetic process | 0.014389 |
| GO:0021700 | developmental maturation | 0.014721 |
| GO:0006469 | negative regulation of protein kinase activity | 0.014756 |
| GO:0002224 | toll-like receptor signaling pathway | 0.014882 |
| GO:0001824 | blastocyst development | 0.015185 |
| GO:0019827 | stem cell maintenance | 0.017202 |
| GO:0050776 | regulation of immune response | 0.019206 |
| GO:0051098 | regulation of binding | 0.019234 |
| GO:0006952 | defense response | 0.019243 |
| GO:0045685 | regulation of glial cell differentiation | 0.019407 |
| GO:0033144 | negative regulation of steroid hormone receptor signaling pathway | 0.02002 |
| GO:0031349 | positive regulation of defense response | 0.020951 |
| GO:0051270 | regulation of cellular component movement | 0.021757 |
| GO:0033673 | negative regulation of kinase activity | 0.0218 |
| GO:0050679 | positive regulation of epithelial cell proliferation | 0.022264 |
| GO:0048864 | stem cell development | 0.023127 |
| GO:0019079 | viral genome replication | 0.024578 |
| GO:0048661 | positive regulation of smooth muscle cell proliferation | 0.024578 |
| GO:0031669 | cellular response to nutrient levels | 0.024976 |
| GO:0045090 | retroviral genome replication | 0.026152 |
| GO:0010638 | positive regulation of organelle organization | 0.026237 |
| GO:0040012 | regulation of locomotion | 0.028014 |
| GO:0048015 | phosphatidylinositol-mediated signaling | 0.028965 |
| GO:0048017 | inositol lipid-mediated signaling | 0.028965 |
| GO:0051049 | regulation of transport | 0.030372 |
| GO:0070979 | protein K11-linked ubiquitination | 0.031271 |
| GO:0048596 | embryonic camera-type eye morphogenesis | 0.03143 |
| GO:0090092 | regulation of transmembrane receptor protein serine/threonine kinase signaling | 0.032492 |

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| | pathway | |
| GO:0010741 | negative regulation of intracellular protein kinase cascade | 0.033756 |
| GO:0060216 | definitive hemopoiesis | 0.035897 |
| GO:0007098 | centrosome cycle | 0.036812 |
| GO:0008635 | activation of caspase activity by cytochrome c | 0.036949 |
| GO:0034770 | histone H4-K20 methylation | 0.036949 |
| GO:0042789 | mRNA transcription from RNA polymerase II promoter | 0.036949 |
| GO:0045821 | positive regulation of glycolysis | 0.036949 |
| GO:0051123 | RNA polymerase II transcriptional preinitiation complex assembly | 0.036949 |
| GO:0051571 | positive regulation of histone H3-K4 methylation | 0.036949 |
| GO:0070897 | DNA-dependent transcriptional preinitiation complex assembly | 0.036949 |
| GO:0090400 | stress-induced premature senescence | 0.036949 |
| GO:2000757 | negative regulation of peptidyl-lysine acetylation | 0.036949 |
| GO:2000772 | regulation of cellular senescence | 0.036949 |
| GO:0007276 | gamete generation | 0.040263 |
| GO:0002684 | positive regulation of immune system process | 0.040982 |
| GO:0022603 | regulation of anatomical structure morphogenesis | 0.042096 |
| GO:0048511 | rhythmic process | 0.043484 |
| GO:0051259 | protein oligomerization | 0.044744 |
| GO:0006305 | DNA alkylation | 0.046015 |
| GO:0006306 | DNA methylation | 0.046015 |
| GO:0002088 | lens development in camera-type eye | 0.046412 |
| GO:0009303 | rRNA transcription | 0.046435 |
| GO:0010907 | positive regulation of glucose metabolic process | 0.046435 |
| GO:0006928 | cellular component movement | 0.048393 |
| GO:0000085 | G2 phase of mitotic cell cycle | 0.050352 |
| GO:0006975 | DNA damage induced protein phosphorylation | 0.050352 |
| GO:0007095 | mitotic cell cycle G2/M transition DNA damage checkpoint | 0.050352 |
| GO:0010870 | positive regulation of receptor biosynthetic process | 0.050352 |
| GO:0051319 | G2 phase | 0.050352 |
| GO:2000036 | regulation of stem cell maintenance | 0.050352 |
| GO:0008543 | fibroblast growth factor receptor signaling pathway | 0.051394 |
| GO:0033500 | carbohydrate homeostasis | 0.051394 |
| GO:0042593 | glucose homeostasis | 0.051394 |
| GO:0048469 | cell maturation | 0.051394 |
| GO:0008406 | gonad development | 0.051738 |
| GO:0030224 | monocyte differentiation | 0.05239 |
| GO:0043388 | positive regulation of DNA binding | 0.05239 |
| GO:0048048 | embryonic eye morphogenesis | 0.052944 |
| GO:0001944 | vasculature development | 0.053333 |
| GO:0009967 | positive regulation of signal transduction | 0.055231 |
| GO:0000724 | double-strand break repair via homologous recombination | 0.056797 |
| GO:0051641 | cellular localization | 0.057323 |
| GO:0005980 | glycogen catabolic process | 0.059033 |
| GO:0071103 | DNA conformation change | 0.059937 |
| GO:0000725 | recombinational repair | 0.060844 |
| GO:0030168 | platelet activation | 0.061366 |
| GO:0017038 | protein import | 0.064129 |
| GO:0071901 | negative regulation of protein serine/threonine kinase activity | 0.064917 |
| GO:0071824 | protein-DNA complex subunit organization | 0.065016 |
| GO:0072593 | reactive oxygen species metabolic process | 0.066173 |
| GO:0009251 | glucan catabolic process | 0.066183 |
| GO:0044247 | cellular polysaccharide catabolic process | 0.066183 |
| GO:0051353 | positive regulation of oxidoreductase activity | 0.066183 |
| GO:0043922 | negative regulation by host of viral transcription | 0.066226 |
| GO:0030221 | basophil differentiation | 0.067852 |
| GO:0090241 | negative regulation of histone H4 acetylation | 0.067852 |
| GO:0006342 | chromatin silencing | 0.07391 |
| GO:0010165 | response to X-ray | 0.07391 |

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| GO:0048732 | gland development | 0.077569 |
| GO:0031100 | organ regeneration | 0.077828 |
| GO:0000723 | telomere maintenance | 0.079186 |
| GO:0006271 | DNA strand elongation involved in DNA replication | 0.08239 |
| GO:0010389 | regulation of G2/M transition of mitotic cell cycle | 0.08239 |
| GO:0032200 | telomere organization | 0.08442 |
| GO:0007088 | regulation of mitosis | 0.085042 |
| GO:0051783 | regulation of nuclear division | 0.085042 |
| GO:0045346 | regulation of MHC class II biosynthetic process | 0.085319 |
| GO:0031667 | response to nutrient levels | 0.086448 |
| GO:0051707 | response to other organism | 0.092595 |
| GO:0043254 | regulation of protein complex assembly | 0.093084 |
| GO:0031076 | embryonic camera-type eye development | 0.095681 |
| GO:0044281 | small molecule metabolic process | 0.099309 |
| GO:0010565 | regulation of cellular ketone metabolic process | 0.099461 |
| GO:0051591 | response to cAMP | 0.101279 |
| GO:0010833 | telomere maintenance via telomere lengthening | 0.101454 |
| GO:0061180 | mammary gland epithelium development | 0.105709 |
| GO:0045471 | response to ethanol | 0.10619 |
| GO:0009299 | mRNA transcription | 0.107743 |
| GO:0045342 | MHC class II biosynthetic process | 0.107743 |
| GO:0046886 | positive regulation of hormone biosynthetic process | 0.107743 |
| GO:0002253 | activation of immune response | 0.107852 |
| GO:0061061 | muscle structure development | 0.108825 |
| GO:0031099 | regeneration | 0.109074 |
| GO:0050778 | positive regulation of immune response | 0.110754 |
| GO:0010226 | response to lithium ion | 0.111862 |
| GO:0022616 | DNA strand elongation | 0.111862 |
| GO:0051412 | response to corticosterone stimulus | 0.111862 |
| GO:0043433 | negative regulation of sequence-specific DNA binding transcription factor activity | 0.114705 |
| GO:0045137 | development of primary sexual characteristics | 0.116568 |
| GO:0048562 | embryonic organ morphogenesis | 0.119163 |
| GO:0010647 | positive regulation of cell communication | 0.119214 |
| GO:0032496 | response to lipopolysaccharide | 0.121768 |
| GO:0023056 | positive regulation of signaling | 0.12202 |
| GO:0006955 | immune response | 0.122188 |
| GO:0000226 | microtubule cytoskeleton organization | 0.123108 |
| GO:0006312 | mitotic recombination | 0.123108 |
| GO:0010039 | response to iron ion | 0.123108 |
| GO:0045600 | positive regulation of fat cell differentiation | 0.123108 |
| GO:0019216 | regulation of lipid metabolic process | 0.123903 |
| GO:0048709 | oligodendrocyte differentiation | 0.129613 |
| GO:0031062 | positive regulation of histone methylation | 0.13329 |
| GO:0032897 | negative regulation of viral transcription | 0.13329 |
| GO:0001568 | blood vessel development | 0.138973 |
| GO:0042692 | muscle cell differentiation | 0.139671 |
| GO:0032881 | regulation of polysaccharide metabolic process | 0.162642 |
| GO:0070873 | regulation of glycogen metabolic process | 0.162642 |
| GO:0018022 | peptidyl-lysine methylation | 0.162818 |
| GO:0060260 | regulation of transcription initiation from RNA polymerase II promoter | 0.162818 |
| GO:0071850 | mitotic cell cycle arrest | 0.162818 |
| GO:2000378 | negative regulation of reactive oxygen species metabolic process | 0.162818 |
| GO:0002526 | acute inflammatory response | 0.164408 |
| GO:0071845 | cellular component disassembly at cellular level | 0.167193 |
| GO:0051385 | response to mineralocorticoid stimulus | 0.177245 |
| GO:0048870 | cell motility | 0.178205 |
| GO:0051674 | localization of cell | 0.178205 |
| GO:0022411 | cellular component disassembly | 0.18143 |

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| GO:0010676 | positive regulation of cellular carbohydrate metabolic process | 0.193056 |
| GO:0045913 | positive regulation of carbohydrate metabolic process | 0.193056 |
| GO:0007389 | pattern specification process | 0.195836 |
| GO:0070076 | histone lysine demethylation | 0.196156 |
| GO:0002237 | response to molecule of bacterial origin | 0.196727 |
| GO:0006344 | maintenance of chromatin silencing | 0.197492 |
| GO:0021537 | telencephalon development | 0.197492 |
| GO:0021603 | cranial nerve formation | 0.197492 |
| GO:0032071 | regulation of endodeoxyribonuclease activity | 0.197492 |
| GO:0051097 | negative regulation of helicase activity | 0.197492 |
| GO:2000773 | negative regulation of cellular senescence | 0.197492 |
| GO:0051100 | negative regulation of binding | 0.198361 |
| GO:0006954 | inflammatory response | 0.212506 |
| GO:0033036 | macromolecule localization | 0.214877 |
| GO:0045839 | negative regulation of mitosis | 0.227229 |
| GO:0051784 | negative regulation of nuclear division | 0.227229 |
| GO:0006289 | nucleotide-excision repair | 0.231437 |
| GO:0006368 | transcription elongation from RNA polymerase II promoter | 0.231437 |
| GO:0008286 | insulin receptor signaling pathway | 0.231438 |
| GO:0071902 | positive regulation of protein serine/threonine kinase activity | 0.232658 |
| GO:0032352 | positive regulation of hormone metabolic process | 0.233011 |
| GO:0043353 | enucleate erythrocyte differentiation | 0.233011 |
| GO:0006333 | chromatin assembly or disassembly | 0.23785 |
| GO:0045862 | positive regulation of proteolysis | 0.243059 |
| GO:0007005 | mitochondrion organization | 0.254777 |
| GO:0051147 | regulation of muscle cell differentiation | 0.25521 |
| GO:0033574 | response to testosterone stimulus | 0.265809 |
| GO:0006304 | DNA modification | 0.268043 |
| GO:0045664 | regulation of neuron differentiation | 0.274122 |
| GO:0006359 | regulation of transcription from RNA polymerase III promoter | 0.274339 |
| GO:0010390 | histone monoubiquitination | 0.274339 |
| GO:0030949 | positive regulation of vascular endothelial growth factor receptor signaling pathway | 0.274339 |
| GO:0031065 | positive regulation of histone deacetylation | 0.274339 |
| GO:0061029 | eyelid development in camera-type eye | 0.274339 |
| GO:2000142 | regulation of transcription initiation, DNA-dependent | 0.274339 |
| GO:0045087 | innate immune response | 0.280189 |
| GO:0007548 | sex differentiation | 0.284003 |
| GO:0045687 | positive regulation of glial cell differentiation | 0.286002 |
| GO:0060749 | mammary gland alveolus development | 0.286002 |
| GO:0061377 | mammary gland lobule development | 0.286002 |
| GO:0003006 | developmental process involved in reproduction | 0.297444 |
| GO:0048010 | vascular endothelial growth factor receptor signaling pathway | 0.308521 |
| GO:0006301 | postreplication repair | 0.32051 |
| GO:0016577 | histone demethylation | 0.32051 |
| GO:0009266 | response to temperature stimulus | 0.324116 |
| GO:0045667 | regulation of osteoblast differentiation | 0.324116 |
| GO:0032880 | regulation of protein localization | 0.329993 |
| GO:0051240 | positive regulation of multicellular organismal process | 0.334947 |
| GO:0008104 | protein localization | 0.337283 |
| GO:0051297 | centrosome organization | 0.338293 |
| GO:0006605 | protein targeting | 0.348237 |
| GO:0045598 | regulation of fat cell differentiation | 0.354177 |
| GO:0006482 | protein demethylation | 0.370962 |
| GO:0008214 | protein dealkylation | 0.370962 |
| GO:0033158 | regulation of protein import into nucleus, translocation | 0.370962 |
| GO:0045922 | negative regulation of fatty acid metabolic process | 0.370962 |
| GO:0071285 | cellular response to lithium ion | 0.370962 |
| GO:0006006 | glucose metabolic process | 0.374359 |

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| GO:0060041 | retina development in camera-type eye | 0.381854 |
| GO:0001835 | blastocyst hatching | 0.385183 |
| GO:0034773 | histone H4-K20 trimethylation | 0.385183 |
| GO:0035188 | hatching | 0.385183 |
| GO:0044026 | DNA hypermethylation | 0.385183 |
| GO:0044027 | hypermethylation of CpG island | 0.385183 |
| GO:0071684 | organism emergence from protective structure | 0.385183 |
| GO:2000774 | positive regulation of cellular senescence | 0.385183 |
| GO:0031023 | microtubule organizing center organization | 0.403128 |
| GO:0009913 | epidermal cell differentiation | 0.405823 |
| GO:0032436 | positive regulation of proteasomal ubiquitin-dependent protein catabolic process | 0.407892 |
| GO:0048608 | reproductive structure development | 0.42292 |
| GO:0031063 | regulation of histone deacetylation | 0.424444 |
| GO:0032459 | regulation of protein oligomerization | 0.424444 |
| GO:0043618 | regulation of transcription from RNA polymerase II promoter in response to stress | 0.424444 |
| GO:0045736 | negative regulation of cyclin-dependent protein kinase activity | 0.424444 |
| GO:0060644 | mammary gland epithelial cell differentiation | 0.424444 |
| GO:2000736 | regulation of stem cell differentiation | 0.424444 |
| GO:0070201 | regulation of establishment of protein localization | 0.429652 |
| GO:0000060 | protein import into nucleus, translocation | 0.435808 |
| GO:0005977 | glycogen metabolic process | 0.438363 |
| GO:2000177 | regulation of neural precursor cell proliferation | 0.438363 |
| GO:0060341 | regulation of cellular localization | 0.446491 |
| GO:0006073 | cellular glucan metabolic process | 0.457482 |
| GO:0044042 | glucan metabolic process | 0.457482 |
| GO:0006336 | DNA replication-independent nucleosome assembly | 0.484211 |
| GO:0034080 | CenH3-containing nucleosome assembly at centromere | 0.484211 |
| GO:0034724 | DNA replication-independent nucleosome organization | 0.484211 |
| GO:0060395 | SMAD protein signal transduction | 0.484211 |
| GO:0016071 | mRNA metabolic process | 0.486056 |
| GO:0006521 | regulation of cellular amino acid metabolic process | 0.529416 |
| GO:0048713 | regulation of oligodendrocyte differentiation | 0.529416 |
| GO:0035239 | tube morphogenesis | 0.530803 |
| GO:0001779 | natural killer cell differentiation | 0.550045 |
| GO:0032201 | telomere maintenance via semi-conservative replication | 0.550045 |
| GO:0071157 | negative regulation of cell cycle arrest | 0.550045 |
| GO:0030183 | B cell differentiation | 0.562651 |
| GO:0051649 | establishment of localization in cell | 0.56824 |
| GO:0045732 | positive regulation of protein catabolic process | 0.585692 |
| GO:0045995 | regulation of embryonic development | 0.585692 |
| GO:0006110 | regulation of glycolysis | 0.621277 |
| GO:0006361 | transcription initiation from RNA polymerase I promoter | 0.621277 |
| GO:0090312 | positive regulation of protein deacetylation | 0.621277 |
| GO:0061030 | epithelial cell differentiation involved in mammary gland alveolus development | 0.630571 |
| GO:0046677 | response to antibiotic | 0.635734 |
| GO:0031055 | chromatin remodeling at centromere | 0.69737 |
| GO:0003151 | outflow tract morphogenesis | 0.71573 |
| GO:0014015 | positive regulation of gliogenesis | 0.71573 |
| GO:0045740 | positive regulation of DNA replication | 0.71573 |
| GO:0000722 | telomere maintenance via recombination | 0.77927 |
| GO:0019433 | triglyceride catabolic process | 0.77927 |
| GO:0043620 | regulation of DNA-dependent transcription in response to stress | 0.77927 |
| GO:0046885 | regulation of hormone biosynthetic process | 0.77927 |
| GO:0006997 | nucleus organization | 0.80152 |
| GO:0018107 | peptidyl-threonine phosphorylation | 0.80152 |
| GO:0071383 | cellular response to steroid hormone stimulus | 0.80152 |
| GO:0030098 | lymphocyte differentiation | 0.804387 |
| GO:0007249 | I-kappaB kinase/NF-kappaB cascade | 0.808347 |

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|------------|--|----------|
| GO:0046777 | protein autophosphorylation | 0.808347 |
| GO:0051179 | localization | 0.81824 |
| GO:0033273 | response to vitamin | 0.826112 |
| GO:0042110 | T cell activation | 0.827189 |
| GO:0050864 | regulation of B cell activation | 0.854843 |
| GO:0006278 | RNA-dependent DNA replication | 0.865745 |
| GO:0070303 | negative regulation of stress-activated protein kinase signaling cascade | 0.865745 |
| GO:0002683 | negative regulation of immune system process | 0.90119 |
| GO:0000302 | response to reactive oxygen species | 0.913287 |
| GO:0007173 | epidermal growth factor receptor signaling pathway | 0.913287 |
| GO:0051099 | positive regulation of binding | 0.918534 |
| GO:0032873 | negative regulation of stress-activated MAPK cascade | 0.930108 |
| GO:0042791 | 5S class rRNA transcription from RNA polymerase III type 1 promoter | 0.930108 |
| GO:0042797 | tRNA transcription from RNA polymerase III promoter | 0.930108 |
| GO:0045347 | negative regulation of MHC class II biosynthetic process | 0.930108 |
| GO:0046628 | positive regulation of insulin receptor signaling pathway | 0.930108 |
| GO:0006953 | acute-phase response | 0.941532 |
| GO:0018210 | peptidyl-threonine modification | 0.941532 |
| GO:0043486 | histone exchange | 0.958155 |
| GO:0060249 | anatomical structure homeostasis | 0.978948 |
| GO:0016055 | Wnt receptor signaling pathway | 0.985954 |
| GO:0021543 | pallium development | 0.9864 |
| GO:0034613 | cellular protein localization | 0.987784 |
| GO:0006284 | base-excision repair | 0.991478 |
| GO:0030888 | regulation of B cell proliferation | 0.991478 |

Cellular Component

| GO id | GO name | adjusted-P |
|------------|--|------------|
| GO:0031981 | nuclear lumen | 2.56E-120 |
| GO:0044428 | nuclear part | 3.08E-112 |
| GO:0070013 | intracellular organelle lumen | 3.90E-111 |
| GO:0043233 | organelle lumen | 2.68E-110 |
| GO:0031974 | membrane-enclosed lumen | 2.89E-109 |
| GO:0005654 | nucleoplasm | 9.90E-106 |
| GO:0005634 | nucleus | 1.25E-102 |
| GO:0043231 | intracellular membrane-bounded organelle | 4.22E-72 |
| GO:0043227 | membrane-bounded organelle | 7.95E-72 |
| GO:0044446 | intracellular organelle part | 1.32E-65 |
| GO:0044422 | organelle part | 1.86E-64 |
| GO:0043229 | intracellular organelle | 6.35E-62 |
| GO:0043226 | organelle | 1.14E-61 |
| GO:0044424 | intracellular part | 7.73E-59 |
| GO:0044451 | nucleoplasm part | 2.22E-52 |
| GO:0005622 | intracellular | 1.01E-49 |
| GO:0044427 | chromosomal part | 1.24E-42 |
| GO:0005694 | chromosome | 3.40E-42 |
| GO:0000785 | chromatin | 1.49E-37 |
| GO:0043234 | protein complex | 2.10E-36 |
| GO:0032991 | macromolecular complex | 1.44E-35 |
| GO:0005667 | transcription factor complex | 3.55E-34 |
| GO:0000228 | nuclear chromosome | 7.35E-34 |
| GO:0043228 | non-membrane-bounded organelle | 4.12E-33 |
| GO:0043232 | intracellular non-membrane-bounded organelle | 4.12E-33 |
| GO:0044454 | nuclear chromosome part | 1.37E-31 |
| GO:0044464 | cell part | 1.82E-27 |
| GO:0005623 | cell | 1.83E-27 |
| GO:0000790 | nuclear chromatin | 2.80E-25 |
| GO:0005575 | cellular_component | 2.89E-22 |

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|------------|--|----------|
| GO:0005829 | cytosol | 3.19E-21 |
| GO:0005737 | cytoplasm | 1.88E-17 |
| GO:0017053 | transcriptional repressor complex | 1.40E-15 |
| GO:0005730 | nucleolus | 4.73E-15 |
| GO:0000307 | cyclin-dependent protein kinase holoenzyme complex | 6.64E-14 |
| GO:0035097 | histone methyltransferase complex | 1.78E-12 |
| GO:0034708 | methyltransferase complex | 3.65E-12 |
| GO:0016585 | chromatin remodeling complex | 8.14E-12 |
| GO:0016604 | nuclear body | 4.18E-10 |
| GO:0016363 | nuclear matrix | 6.66E-10 |
| GO:0000792 | heterochromatin | 8.27E-10 |
| GO:0034399 | nuclear periphery | 1.89E-09 |
| GO:0016605 | PML body | 1.97E-09 |
| GO:0005657 | replication fork | 2.18E-07 |
| GO:0000118 | histone deacetylase complex | 2.60E-06 |
| GO:0044444 | cytoplasmic part | 3.40E-06 |
| GO:0031519 | PcG protein complex | 4.78E-06 |
| GO:0000775 | chromosome, centromeric region | 7.66E-06 |
| GO:0000791 | euchromatin | 1.37E-05 |
| GO:0000793 | condensed chromosome | 8.77E-05 |
| GO:0005720 | nuclear heterochromatin | 9.71E-05 |
| GO:0016580 | Sin3 complex | 7.32E-04 |
| GO:0035098 | ESC/E(Z) complex | 7.32E-04 |
| GO:0070822 | Sin3-type complex | 7.32E-04 |
| GO:0015630 | microtubule cytoskeleton | 7.36E-04 |
| GO:0035189 | Rb-E2F complex | 0.001326 |
| GO:0005635 | nuclear envelope | 0.003046 |
| GO:0000794 | condensed nuclear chromosome | 0.003677 |
| GO:0005819 | spindle | 0.005484 |
| GO:0005856 | cytoskeleton | 0.006478 |
| GO:0000780 | condensed nuclear chromosome, centromeric region | 0.010029 |
| GO:0005815 | microtubule organizing center | 0.010464 |
| GO:0000152 | nuclear ubiquitin ligase complex | 0.010688 |
| GO:0072357 | PTW/PP1 phosphatase complex | 0.011088 |
| GO:0070688 | MLL5-L complex | 0.017595 |
| GO:0016581 | NuRD complex | 0.02002 |
| GO:0031965 | nuclear membrane | 0.023471 |
| GO:0005813 | centrosome | 0.028432 |
| GO:0000151 | ubiquitin ligase complex | 0.030462 |
| GO:0001940 | male pronucleus | 0.036949 |
| GO:0001939 | female pronucleus | 0.066226 |
| GO:0005719 | nuclear euchromatin | 0.066226 |
| GO:0070557 | PCNA-p21 complex | 0.067852 |
| GO:0005721 | centromeric heterochromatin | 0.085319 |
| GO:0032993 | protein-DNA complex | 0.152255 |
| GO:0044430 | cytoskeletal part | 0.174874 |
| GO:0005680 | anaphase-promoting complex | 0.177245 |
| GO:0005876 | spindle microtubule | 0.245745 |
| GO:0031967 | organelle envelope | 0.364413 |
| GO:0008024 | positive transcription elongation factor complex b | 0.385183 |
| GO:0033553 | rDNA heterochromatin | 0.385183 |
| GO:0000779 | condensed chromosome, centromeric region | 0.477379 |
| GO:0031975 | envelope | 0.487438 |
| GO:0071141 | SMAD protein complex | 0.630571 |
| GO:0000781 | chromosome, telomeric region | 0.635734 |
| GO:0000803 | sex chromosome | 0.69737 |
| GO:0005669 | transcription factor TFIID complex | 0.69737 |
| GO:0045120 | pronucleus | 0.77927 |

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| GO:0071339 | MLL1 complex | 0.77927 |
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Molecular Function

| GO id | GO name | adjusted-P |
|------------|--|------------|
| GO:0005515 | protein binding | 2.29E-84 |
| GO:0008134 | transcription factor binding | 4.56E-57 |
| GO:0044212 | transcription regulatory region DNA binding | 5.55E-40 |
| GO:0000975 | regulatory region DNA binding | 1.59E-38 |
| GO:0001067 | regulatory region nucleic acid binding | 1.59E-38 |
| GO:0003677 | DNA binding | 2.31E-37 |
| GO:0005488 | binding | 1.88E-35 |
| GO:0019899 | enzyme binding | 3.00E-35 |
| GO:0000988 | protein binding transcription factor activity | 1.76E-31 |
| GO:0003712 | transcription cofactor activity | 6.78E-30 |
| GO:0000989 | transcription factor binding transcription factor activity | 1.63E-29 |
| GO:0003700 | sequence-specific DNA binding transcription factor activity | 1.22E-28 |
| GO:0001071 | nucleic acid binding transcription factor activity | 1.40E-28 |
| GO:0003682 | chromatin binding | 5.09E-23 |
| GO:0003676 | nucleic acid binding | 1.52E-21 |
| GO:0003713 | transcription coactivator activity | 9.60E-20 |
| GO:0019901 | protein kinase binding | 2.18E-18 |
| GO:0043565 | sequence-specific DNA binding | 1.53E-17 |
| GO:0000981 | sequence-specific DNA binding RNA polymerase II transcription factor activity | 2.72E-17 |
| GO:0019900 | kinase binding | 1.24E-16 |
| GO:0001085 | RNA polymerase II transcription factor binding | 1.41E-16 |
| GO:0070491 | repressing transcription factor binding | 3.83E-16 |
| GO:0003674 | molecular_function | 3.42E-13 |
| GO:0003714 | transcription corepressor activity | 5.14E-13 |
| GO:0042802 | identical protein binding | 9.08E-13 |
| GO:0042393 | histone binding | 2.97E-12 |
| GO:0002039 | p53 binding | 5.82E-12 |
| GO:0035258 | steroid hormone receptor binding | 8.44E-12 |
| GO:0035257 | nuclear hormone receptor binding | 1.80E-11 |
| GO:0051427 | hormone receptor binding | 2.35E-10 |
| GO:0046983 | protein dimerization activity | 2.74E-10 |
| GO:0035326 | enhancer binding | 1.09E-08 |
| GO:0003705 | sequence-specific enhancer binding RNA polymerase II transcription factor activity | 1.28E-08 |
| GO:0001047 | core promoter binding | 1.83E-08 |
| GO:0042826 | histone deacetylase binding | 2.35E-08 |
| GO:0019904 | protein domain specific binding | 2.44E-08 |
| GO:0031625 | ubiquitin protein ligase binding | 3.05E-08 |
| GO:0050681 | androgen receptor binding | 1.01E-07 |
| GO:0004693 | cyclin-dependent protein kinase activity | 1.22E-07 |
| GO:0001158 | enhancer sequence-specific DNA binding | 2.10E-07 |
| GO:0000976 | transcription regulatory region sequence-specific DNA binding | 2.99E-07 |
| GO:0001012 | RNA polymerase II regulatory region DNA binding | 4.12E-07 |
| GO:0043566 | structure-specific DNA binding | 5.03E-07 |
| GO:0035064 | methylated histone residue binding | 2.38E-06 |
| GO:0046332 | SMAD binding | 4.13E-06 |
| GO:0042803 | protein homodimerization activity | 4.61E-06 |
| GO:0000977 | RNA polymerase II regulatory region sequence-specific DNA binding | 5.27E-06 |

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| GO:0000982 | RNA polymerase II core promoter proximal region sequence-specific DNA binding transcription factor activity | 6.44E-06 |
| GO:0035035 | histone acetyltransferase binding | 8.73E-06 |
| GO:0001103 | RNA polymerase II repressing transcription factor binding | 1.10E-05 |
| GO:0035497 | cAMP response element binding | 2.32E-05 |
| GO:0046982 | protein heterodimerization activity | 5.53E-05 |
| GO:0001077 | RNA polymerase II core promoter proximal region sequence-specific DNA binding transcription factor activity involved in positive regulation of transcription | 8.16E-05 |
| GO:0043425 | bHLH transcription factor binding | 9.06E-05 |
| GO:0000980 | RNA polymerase II enhancer sequence-specific DNA binding | 1.02E-04 |
| GO:0004674 | protein serine/threonine kinase activity | 1.51E-04 |
| GO:0030332 | cyclin binding | 1.72E-04 |
| GO:0016538 | cyclin-dependent protein kinase regulator activity | 4.21E-04 |
| GO:0008757 | S-adenosylmethionine-dependent methyltransferase activity | 5.67E-04 |
| GO:0004672 | protein kinase activity | 6.06E-04 |
| GO:0033613 | activating transcription factor binding | 6.67E-04 |
| GO:0016773 | phosphotransferase activity, alcohol group as acceptor | 6.93E-04 |
| GO:0005102 | receptor binding | 9.68E-04 |
| GO:0042054 | histone methyltransferase activity | 0.001009 |
| GO:0032129 | histone deacetylase activity (H3-K9 specific) | 0.001457 |
| GO:0046969 | NAD-dependent histone deacetylase activity (H3-K9 specific) | 0.001457 |
| GO:0008022 | protein C-terminus binding | 0.001498 |
| GO:0004842 | ubiquitin-protein ligase activity | 0.001813 |
| GO:0016301 | kinase activity | 0.002189 |
| GO:0019207 | kinase regulator activity | 0.00224 |
| GO:0017136 | NAD-dependent histone deacetylase activity | 0.002608 |
| GO:0034979 | NAD-dependent protein deacetylase activity | 0.002608 |
| GO:0001078 | RNA polymerase II core promoter proximal region sequence-specific DNA binding transcription factor activity involved in negative regulation of transcription | 0.002616 |
| GO:0019787 | small conjugating protein ligase activity | 0.0035 |
| GO:0003690 | double-stranded DNA binding | 0.003949 |
| GO:0000987 | core promoter proximal region sequence-specific DNA binding | 0.004307 |
| GO:0008170 | N-methyltransferase activity | 0.00462 |
| GO:0001159 | core promoter proximal region DNA binding | 0.004655 |
| GO:0018024 | histone-lysine N-methyltransferase activity | 0.005857 |
| GO:0030957 | Tat protein binding | 0.006419 |
| GO:0035173 | histone kinase activity | 0.006735 |
| GO:0016278 | lysine N-methyltransferase activity | 0.008395 |
| GO:0016279 | protein-lysine N-methyltransferase activity | 0.008395 |
| GO:0008276 | protein methyltransferase activity | 0.010676 |
| GO:0001106 | RNA polymerase II transcription corepressor activity | 0.02002 |
| GO:0070888 | E-box binding | 0.020693 |
| GO:0016772 | transferase activity, transferring phosphorus-containing groups | 0.025626 |
| GO:0008301 | DNA bending activity | 0.03143 |
| GO:0042974 | retinoic acid receptor binding | 0.046015 |
| GO:0008094 | DNA-dependent ATPase activity | 0.051185 |
| GO:0001102 | RNA polymerase II activating transcription factor binding | 0.05239 |
| GO:0019887 | protein kinase regulator activity | 0.055265 |
| GO:0016881 | acid-amino acid ligase activity | 0.060825 |
| GO:0031078 | histone deacetylase activity (H3-K14 specific) | 0.066226 |
| GO:0032041 | NAD-dependent histone deacetylase activity (H3-K14 specific) | 0.066226 |
| GO:0046970 | NAD-dependent histone deacetylase activity (H4-K16 specific) | 0.066226 |

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| GO:0031493 | nucleosomal histone binding | 0.067852 |
| GO:0004197 | cysteine-type endopeptidase activity | 0.07861 |
| GO:0046872 | metal ion binding | 0.081449 |
| GO:0016740 | transferase activity | 0.107061 |
| GO:0043169 | cation binding | 0.138419 |
| GO:0043167 | ion binding | 0.145099 |
| GO:0004861 | cyclin-dependent protein kinase inhibitor activity | 0.162818 |
| GO:0008353 | RNA polymerase II carboxy-terminal domain kinase activity | 0.162818 |
| GO:0003824 | catalytic activity | 0.180336 |
| GO:0032452 | histone demethylase activity | 0.196156 |
| GO:0008270 | zinc ion binding | 0.197044 |
| GO:0070644 | vitamin D response element binding | 0.197492 |
| GO:0001076 | RNA polymerase II transcription factor binding transcription factor activity | 0.21348 |
| GO:0000979 | RNA polymerase II core promoter sequence-specific DNA binding | 0.245745 |
| GO:0016879 | ligase activity, forming carbon-nitrogen bonds | 0.246898 |
| GO:0004407 | histone deacetylase activity | 0.286002 |
| GO:0030374 | ligand-dependent nuclear receptor transcription coactivator activity | 0.286002 |
| GO:0030971 | receptor tyrosine kinase binding | 0.381996 |
| GO:0033558 | protein deacetylase activity | 0.381996 |
| GO:0034648 | histone demethylase activity (H3-dimethyl-K4 specific) | 0.385183 |
| GO:0051525 | NFAT protein binding | 0.385183 |
| GO:0004860 | protein kinase inhibitor activity | 0.407892 |
| GO:0047485 | protein N-terminus binding | 0.438363 |
| GO:0019210 | kinase inhibitor activity | 0.465332 |
| GO:0008168 | methyltransferase activity | 0.615456 |
| GO:0003886 | DNA (cytosine-5-)-methyltransferase activity | 0.630571 |
| GO:0043125 | ErbB-3 class receptor binding | 0.630571 |
| GO:0001046 | core promoter sequence-specific DNA binding | 0.635734 |
| GO:0070412 | R-SMAD binding | 0.69737 |
| GO:0032451 | demethylase activity | 0.77927 |
| GO:0001104 | RNA polymerase II transcription cofactor activity | 0.79583 |
| GO:0008234 | cysteine-type peptidase activity | 0.804387 |
| GO:0009008 | DNA-methyltransferase activity | 0.930108 |
| GO:0019213 | deacetylase activity | 0.991478 |

Table S14. Interactors of human p107

| Gene Name | Protein Name | Description (from NCBI Gene database) |
|-----------|---|--|
| AATF | apoptosis antagonizing transcription factor | <i>See table S12</i> |
| ARID4A | AT rich interactive domain 4A (RBP1-like) | <i>See table S12</i> |
| BEGAIN | brain-enriched guanylate kinase-associated homolog | May sustain the structure of the postsynaptic density (PSD). |
| BRCA1 | breast cancer 1, early onset | <i>See table S12</i> |
| BRF1 | BRF1 homolog, subunit of RNA polymerase III transcription initiation factor IIIB (<i>S. cerevisiae</i>) | <i>See table S12</i> |
| CCNA1 | cyclin A1 | <i>See table S12</i> |
| CCNA2 | cyclin A2 | <i>See table S12</i> |
| CCNE1 | cyclin E1 | <i>See table S12</i> |
| CDK2 | cyclin-dependent kinase 2 | <i>See table S12</i> |
| CDKN1C | cyclin-dependent kinase inhibitor 1C (p57, Kip2) | This gene is imprinted, with preferential expression of the maternal allele. The encoded protein is a tight-binding, strong inhibitor of several G1 cyclin/Cdk complexes and a negative regulator of cell proliferation. Mutations in this gene are implicated in sporadic cancers and Beckwith-Wiedemann syndrome, suggesting that this gene is a tumor suppressor candidate. |
| CREG1 | cellular repressor of E1A-stimulated genes 1 | <i>See table S12</i> |
| DHX30 | DEAH (Asp-Glu-Ala-His) box polypeptide 30 | DEAD box proteins, characterized by the conserved motif Asp-Glu-Ala-Asp (DEAD), are putative RNA helicases. They are implicated in a number of cellular processes involving alteration of RNA secondary structure such as translation initiation, nuclear and mitochondrial splicing, and ribosome and spliceosome assembly. Based on their distribution patterns, some members of this DEAD box protein family are believed to be involved in embryogenesis, spermatogenesis, and cellular growth and division. This gene encodes a member of this family. The encoded protein has 97% sequence identity with the mouse HELG protein. |
| E2F1 | E2F transcription factor 1 | <i>See table S12</i> |
| E2F3 | E2F transcription factor 3 | <i>See table S12</i> |
| E2F4 | E2F transcription factor 4, p107/p130-binding | <i>See table S12</i> |
| E2F5 | E2F transcription factor 5, p130-binding | This protein is differentially phosphorylated and is expressed in a wide variety of human tissues. It has higher identity to E2F4 than to other family members. Both this protein and E2F4 interact with tumor suppressor proteins p130 and p107, but not with pRB. |
| EMD | emerin | Emerin is a serine-rich nuclear membrane protein and a member of the nuclear lamina-associated protein family. It mediates membrane anchorage to the cytoskeleton. Dreifuss-Emery muscular dystrophy is an X-linked inherited degenerative myopathy resulting from mutation in the emerin gene. |
| HDAC1 | histone deacetylase 1 | <i>See table S12</i> |
| HDAC2 | histone deacetylase 2 | <i>See table S12</i> |
| HDAC3 | histone deacetylase 3 | <i>See table S12</i> |
| IRF3 | interferon regulatory factor 3 | <i>See table S12</i> |
| KDM5A | lysine (K)-specific demethylase 5A | <i>See table S12</i> |
| LIN37 | lin-37 homolog (<i>C. elegans</i>) | <i>See table S12</i> |
| LIN54 | lin-54 homolog (<i>C. elegans</i>) | <i>See table S12</i> |

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|---------|---|---|
| LIN9 | lin-9 homolog (<i>C. elegans</i>) | <i>See table S12</i> |
| MAPK6 | mitogen-activated protein kinase 6 | The protein encoded by this gene is a member of the Ser/Thr protein kinase family, and is most closely related to mitogen-activated protein kinases (MAP kinases). MAP kinases also known as extracellular signal-regulated kinases (ERKs), are activated through protein phosphorylation cascades and act as integration points for multiple biochemical signals. This kinase is localized in the nucleus, and has been reported to be activated in fibroblasts upon treatment with serum or phorbol esters. |
| MCM7 | minichromosome maintenance complex component 7 | <i>See table S12</i> |
| MYBL2 | v-mybmyeloblastosis viral oncogene homolog (avian)-like 2 | The protein encoded by this gene, a member of the MYB family of transcription factor genes, is a nuclear protein involved in cell cycle progression. The encoded protein is phosphorylated by cyclin A/cyclin-dependent kinase 2 during the S-phase of the cell cycle and possesses both activator and repressor activities. It has been shown to activate the cell division cycle 2, cyclin D1, and insulin-like growth factor-binding protein 5 genes. |
| MYC | v-mycmyelocytomatosis viral oncogene homolog (avian) | <i>See table S12</i> |
| NR2E3 | nuclear receptor subfamily 2, group E, member 3 | This protein is part of a large family of nuclear receptor transcription factors involved in signaling pathways. Nuclear receptors have been shown to regulate pathways involved in embryonic development, as well as in maintenance of proper cell function in adults. Members of this family are characterized by discrete domains that function in DNA and ligand binding. This gene encodes a retinal nuclear receptor that is a ligand-dependent transcription factor. |
| PHB | prohibitin | <i>See table S12</i> |
| PPP1CA | protein phosphatase 1, catalytic subunit, alpha isozyme | <i>See table S12</i> |
| PPP2R3A | protein phosphatase 2, regulatory subunit B", alpha | This gene encodes one of the regulatory subunits of the protein phosphatase 2. Protein phosphatase 2 (formerly named type 2A) is one of the four major Ser/Thr phosphatases and is implicated in the negative control of cell growth and division. Protein phosphatase 2 holoenzymes are heterotrimeric proteins composed of a structural subunit A, a catalytic subunit C, and a regulatory subunit B. The regulatory subunit is encoded by a diverse set of genes that have been grouped into the B/PR55, B'/PR61, and B''/PR72 families. These different regulatory subunits confer distinct enzymatic specificities and intracellular localizations to the holoenzyme. The product of this gene belongs to the B'' family. The B'' family has been further divided into subfamilies. The product of this gene belongs to the alpha subfamily of regulatory subunit B''. Alternative splicing results in multiple transcript variants encoding different isoforms. |
| RB1 | retinoblastoma 1 | The protein encoded by this gene is a negative regulator of the cell cycle and was the first tumor suppressor gene found. The encoded protein also stabilizes constitutive heterochromatin to maintain the overall chromatin structure. The active, hypophosphorylated form of the protein binds transcription factor E2F1. Defects in this gene are a cause of childhood cancer retinoblastoma (RB), bladder cancer, and osteogenic sarcoma. |
| RBBP8 | retinoblastoma binding protein 8 | <i>See table S12</i> |
| RBBP9 | retinoblastoma binding protein 9 | <i>See table S12</i> |
| RBL2 | retinoblastoma-like 2 (p130) | <i>See table S12</i> |
| SMAD3 | SMAD family member 3 | The protein belongs to the SMAD, a family of proteins similar to the gene products of the <i>Drosophila</i> gene 'mothers against decapentaplegic' (Mad) and the <i>C. elegans</i> gene Sma. SMAD proteins are signal transducers and transcriptional modulators that mediate multiple |

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|---------|---|--|
| | | signaling pathways. This protein functions as a transcriptional modulator activated by transforming growth factor-beta and is thought to play a role in the regulation of carcinogenesis. |
| SMAD4 | SMAD family member 4 | Smad proteins are phosphorylated and activated by transmembrane serine-threonine receptor kinases in response to TGF-beta signaling. The product of this gene forms homomeric complexes and heteromeric complexes with other activated Smad proteins, which then accumulate in the nucleus and regulate the transcription of target genes. This protein binds to DNA and recognizes an 8-bp palindromic sequence (GTCTAGAC) called the Smad-binding element (SBE). The Smad proteins are subject to complex regulation by post-translational modifications. Mutations or deletions in this gene have been shown to result in pancreatic cancer, juvenile polyposis syndrome, and hereditary hemorrhagic telangiectasia syndrome. |
| SMARCA4 | SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4 | <i>See table S12</i> |
| SNW1 | SNW domain containing 1 | <i>See table S12</i> |
| SUMO2 | SMT3 suppressor of mif two 3 homolog 2 (S. cerevisiae) | The protein is a member of the SUMO protein family. It functions in a manner similar to ubiquitin in that it is bound to target proteins as part of a post-translational modification system. However, unlike ubiquitin which targets proteins for degradation, this protein is involved in a variety of cellular processes, such as nuclear transport, transcriptional regulation, apoptosis, and protein stability. It is not active until the last two amino acids of the carboxy-terminus have been cleaved off. Numerous pseudogenes have been reported for this gene. |
| SUMO3 | SMT3 suppressor of mif two 3 homolog 3 (S. cerevisiae) | SUMO proteins, such as SUMO3, and ubiquitin posttranslationally modify numerous cellular proteins and affect their metabolism and function. However, unlike ubiquitination, which targets proteins for degradation, sumoylation participates in a number of cellular processes, such as nuclear transport, transcriptional regulation, apoptosis, and protein stability. |
| SUV39H1 | suppressor of variegation 3-9 homolog 1 (Drosophila) | <i>See table S12</i> |
| TAF1 | TAF1 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 250kDa | <i>See table S12</i> |
| TFDP1 | transcription factor Dp-1 | <i>See table S12</i> |
| TFDP2 | transcription factor Dp-2 (E2F dimerization partner 2) | <i>See table S12</i> |
| TOP1 | topoisomerase (DNA) I | DNA topoisomerase controls and alters the topologic states of DNA during transcription. This enzyme catalyzes the transient breaking and rejoining of a single strand of DNA, which allows the strands to pass through one another, thus altering the topology of DNA. |
| UBC | ubiquitin C | <i>See table S12</i> |
| USP4 | ubiquitin specific peptidase 4 (proto-oncogene) | <i>See table S12</i> |

Table S15. Interactors of human p130

| Gene Name | Protein Name | Description (from NCBI Gene database) |
|-----------|---|--|
| AATF | apoptosis antagonizing transcription factor | <i>See table S12</i> |
| BRCA1 | breast cancer 1, early onset | <i>See table S12</i> |
| BRF1 | BRF1 homolog, subunit of RNA polymerase III transcription initiation factor IIIB (<i>S. cerevisiae</i>) | <i>See table S12</i> |
| CCNA1 | cyclin A1 | <i>See table S12</i> |
| CCNA2 | cyclin A2 | <i>See table S12</i> |
| CCNE1 | cyclin E1 | <i>See table S12</i> |
| CDK2 | cyclin-dependent kinase 2 | <i>See table S12</i> |
| CUL1 | cullin 1 | Core component of multiple cullin-RING-based SCF (SKP1-CUL1-F-box protein) E3 ubiquitin-protein ligase complexes, which mediate the ubiquitination of proteins involved in cell cycle progression, signal transduction and transcription. In the SCF complex, serves as a rigid scaffold that organizes the SKP1-F-box protein and RBX1 subunits. May contribute to catalysis through positioning of the substrate and the ubiquitin-conjugating enzyme. The E3 ubiquitin-protein ligase activity of the complex is dependent on the neddylation of the cullin subunit and is inhibited by the association of the deneddylated cullin subunit with TIP120A/CAND1. The functional specificity of the SCF complex depends on the F-box protein as substrate recognition component. SCF(BTRC) and SCF(FBXW11) direct ubiquitination of CTNNB1 and participate in Wnt signaling. |
| E2F4 | E2F transcription factor 4, p107/p130-binding | <i>See table S12</i> |
| E2F5 | E2F transcription factor 5, p130-binding | This protein is differentially phosphorylated and is expressed in a wide variety of human tissues. It has higher identity to E2F4 than to other family members. Both this protein and E2F4 interact with tumor suppressor proteins p130 and p107, but not with pRB. |
| ELAVL1 | ELAV (embryonic lethal, abnormal vision, <i>Drosophila</i>)-like 1 (Hu antigen R) | The protein is a member of the ELAVL protein family. This encoded protein contains 3 RNA-binding domains and binds cis-acting AU-rich elements. It destabilizes mRNAs and thereby regulates gene expression. |
| EZH2 | enhancer of zeste homolog 2 (<i>Drosophila</i>) | The protein is a member of the Polycomb-group (PcG) family. PcG family members form multimeric protein complexes, which are involved in maintaining the transcriptional repressive state of genes over successive cell generations. This protein associates with the embryonic ectoderm development protein, the VAV1 oncoprotein, and the X-linked nuclear protein. This protein may play a role in the hematopoietic and central nervous systems. Multiple alternatively spliced transcript variants encoding distinct isoforms have been identified for this gene. |
| HBP1 | HMG-box transcription factor 1 | <i>See table S12</i> |
| HDAC1 | histone deacetylase 1 | <i>See table S12</i> |
| ID2 | inhibitor of DNA binding 2, dominant negative helix-loop-helix protein | <i>See table S12</i> |

| | | |
|----------|--|--|
| IRF3 | interferon regulatory factor 3 | <i>See table S12</i> |
| LIN37 | lin-37 homolog (C. elegans) | <i>See table S12</i> |
| LIN52 | lin-52 homolog (C. elegans) | LIN52 is a component of the LIN, or DREAM, complex, an essential regulator of cell cycle genes |
| LIN54 | lin-54 homolog (C. elegans) | <i>See table S12</i> |
| LIN9 | lin-9 homolog (C. elegans) | <i>See table S12</i> |
| MCM7 | minichromosome maintenance complex component 7 | <i>See table S12</i> |
| PCBD1 | pterin-4 alpha-carbinolaminatedehydratase/dimerization cofactor of hepatocyte nuclear factor 1 alpha | This gene encodes pterin-4 alpha-carbinolaminatedehydratase, an enzyme involved in phenylalanine hydroxylation. A deficiency of this enzyme leads to hyperphenylalaninemia. The enzyme regulates the homodimerization of the transcription factor hepatocyte nuclear factor 1 (HNF1). |
| PHB | prohibitin | <i>See table S12</i> |
| PPP2CA | protein phosphatase 2, catalytic subunit, alpha isozyme | This gene encodes the phosphatase 2A catalytic subunit. Protein phosphatase 2A is one of the four major Ser/Thr phosphatases, and it is implicated in the negative control of cell growth and division. It consists of a common heteromeric core enzyme, which is composed of a catalytic subunit and a constant regulatory subunit that associates with a variety of regulatory subunits. This gene encodes an alpha isoform of the catalytic subunit. |
| RAF1 | v-raf-1 murine leukemia viral oncogene homolog 1 | <i>See table S12</i> |
| RB1 | retinoblastoma 1 | The protein is a negative regulator of the cell cycle and was the first tumor suppressor gene found. The encoded protein also stabilizes constitutive heterochromatin to maintain the overall chromatin structure. The active, hypophosphorylated form of the protein binds transcription factor E2F1. Defects in this gene are a cause of childhood cancer retinoblastoma (RB), bladder cancer, and osteogenic sarcoma. |
| RBBP4 | retinoblastoma binding protein 4 | <i>See table S12</i> |
| RBBP8 | retinoblastoma binding protein 8 | <i>See table S12</i> |
| RBBP9 | retinoblastoma binding protein 9 | <i>See table S12</i> |
| RBL1 | retinoblastoma-like 1 (p107) | <i>See table S12</i> |
| SERPINB2 | serpin peptidase inhibitor, clade B (ovalbumin), member 2 | <i>See table S12</i> |
| SKP1 | S-phase kinase-associated protein 1 | This gene encodes a component of SCF complexes, which are composed of this protein, cullin 1, a ring-box protein, and one member of the F-box family of proteins. This protein binds directly to the F-box motif found in F-box proteins. SCF complexes are involved in the regulated ubiquitination of specific protein substrates, which targets them for degradation by the proteasome. Specific F-box proteins recognize different target protein(s), and many specific SCF substrates have been identified including regulators of cell cycle progression and development. Studies have also characterized the protein as an RNA polymerase II elongation factor. |
| SKP2 | S-phase kinase-associated protein 2, E3 ubiquitin | <i>See table S12</i> |

| | | |
|---------|---|--|
| | protein ligase | |
| SMARCA4 | SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4 | <i>See table S12</i> |
| SNW1 | SNW domain containing 1 | <i>See table S12</i> |
| SUV39H1 | suppressor of variegation 3-9 homolog 1 (Drosophila) | <i>See table S12</i> |
| TAF1 | TAF1 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 250kDa | <i>See table S12</i> |
| TFDP1 | transcription factor Dp-1 | <i>See table S12</i> |
| TFDP2 | transcription factor Dp-2 (E2F dimerization partner 2) | <i>See table S12</i> |
| TOP1 | topoisomerase (DNA) I | This gene encodes a DNA topoisomerase, an enzyme that controls and alters the topologic states of DNA during transcription. This enzyme catalyzes the transient breaking and rejoining of a single strand of DNA which allows the strands to pass through one another, thus altering the topology of DNA. This gene is localized to chromosome 20 and has pseudogenes which reside on chromosomes 1 and 22. |
| TP63 | tumor protein p63 | This gene encodes a member of the p53 family of transcription factors. An animal model, p63 ^{-/-} mice, has been useful in defining the role this protein plays in the development and maintenance of stratified epithelial tissues. p63 ^{-/-} mice have several developmental defects which include the lack of limbs and other tissues, such as teeth and mammary glands, which develop as a result of interactions between mesenchyme and epithelium. Mutations in this gene are associated with ectodermal dysplasia, and cleft lip/palate syndrome 3 (EEC3); split-hand/foot malformation 4 (SHFM4); ankyloblepharon-ectodermal defects-cleft lip/palate; ADULT syndrome (acro-dermato-ungual-lacrima-tooth); limb-mammary syndrome; Rap-Hodgkin syndrome (RHS); and orofacial cleft 8. |
| UBC | ubiquitin C | <i>See table S12</i> |
| USP4 | ubiquitin specific peptidase 4 (proto-oncogene) | <i>See table S12</i> |
| XBP1 | X-box binding protein 1 | The transcription factor regulates MHC class II genes by binding to a promoter element referred to as an X box. This gene product is a bZIP protein, which was also identified as a cellular transcription factor that binds to an enhancer in the promoter of the T cell leukemia virus type 1 promoter. It may increase expression of viral proteins by acting as the DNA binding partner of a viral transactivator. It has been found that upon accumulation of unfolded proteins in the endoplasmic reticulum (ER), the mRNA of this gene is processed to an active form by an unconventional splicing mechanism that is mediated by the endonuclease inositol-requiring enzyme 1 (IRE1). |

Table S16. GO term enrichment of human p107 interactors**Biological Process**

| GO id | GO name | adjusted-P |
|--------------|--|-------------------|
| GO:0007049 | cell cycle | 4.47E-28 |
| GO:0000278 | mitotic cell cycle | 5.07E-27 |
| GO:0006366 | transcription from RNA polymerase II promoter | 4.14E-23 |
| GO:0034645 | cellular macromolecule biosynthetic process | 8.58E-21 |
| GO:0045893 | positive regulation of transcription, DNA-dependent | 1.07E-20 |
| GO:0009059 | macromolecule biosynthetic process | 1.89E-20 |
| GO:0051254 | positive regulation of RNA metabolic process | 2.46E-20 |
| GO:0006351 | transcription, DNA-dependent | 2.79E-20 |
| GO:0000080 | G1 phase of mitotic cell cycle | 3.38E-20 |
| GO:0051329 | interphase of mitotic cell cycle | 4.53E-20 |
| GO:0032774 | RNA biosynthetic process | 4.98E-20 |
| GO:0051318 | G1 phase | 5.63E-20 |
| GO:0051325 | interphase | 6.12E-20 |
| GO:0010628 | positive regulation of gene expression | 7.42E-20 |
| GO:2000112 | regulation of cellular macromolecule biosynthetic process | 7.77E-20 |
| GO:0006355 | regulation of transcription, DNA-dependent | 1.37E-19 |
| GO:0010556 | regulation of macromolecule biosynthetic process | 1.37E-19 |
| GO:0045935 | positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 1.65E-19 |
| GO:0060255 | regulation of macromolecule metabolic process | 1.81E-19 |
| GO:0010557 | positive regulation of macromolecule biosynthetic process | 1.82E-19 |
| GO:0051173 | positive regulation of nitrogen compound metabolic process | 2.53E-19 |
| GO:0051252 | regulation of RNA metabolic process | 3.20E-19 |
| GO:0080090 | regulation of primary metabolic process | 5.76E-19 |
| GO:0031326 | regulation of cellular biosynthetic process | 6.83E-19 |
| GO:0010468 | regulation of gene expression | 7.73E-19 |
| GO:0031328 | positive regulation of cellular biosynthetic process | 8.45E-19 |
| GO:0006357 | regulation of transcription from RNA polymerase II promoter | 8.68E-19 |
| GO:0009889 | regulation of biosynthetic process | 8.84E-19 |
| GO:0031323 | regulation of cellular metabolic process | 8.97E-19 |
| GO:0010604 | positive regulation of macromolecule metabolic process | 8.98E-19 |
| GO:0009891 | positive regulation of biosynthetic process | 1.16E-18 |
| GO:0044260 | cellular macromolecule metabolic process | 1.54E-18 |
| GO:0019222 | regulation of metabolic process | 1.57E-18 |
| GO:0090304 | nucleic acid metabolic process | 1.65E-18 |
| GO:0022402 | cell cycle process | 2.24E-18 |
| GO:0009893 | positive regulation of metabolic process | 5.44E-18 |
| GO:0031325 | positive regulation of cellular metabolic process | 2.05E-17 |
| GO:0019219 | regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 2.16E-17 |
| GO:0016070 | RNA metabolic process | 3.24E-17 |

| | | |
|------------|--|----------|
| GO:0051171 | regulation of nitrogen compound metabolic process | 3.71E-17 |
| GO:0044249 | cellular biosynthetic process | 5.43E-17 |
| GO:0022403 | cell cycle phase | 1.50E-16 |
| GO:0009058 | biosynthetic process | 1.59E-16 |
| GO:0010467 | gene expression | 2.34E-16 |
| GO:0006352 | transcription initiation, DNA-dependent | 4.93E-16 |
| GO:0043170 | macromolecule metabolic process | 6.25E-16 |
| GO:0006367 | transcription initiation from RNA polymerase II promoter | 6.26E-16 |
| GO:0006139 | nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 7.47E-16 |
| GO:0051726 | regulation of cell cycle | 1.87E-15 |
| GO:0034641 | cellular nitrogen compound metabolic process | 2.09E-14 |
| GO:0006807 | nitrogen compound metabolic process | 6.05E-14 |
| GO:0007179 | transforming growth factor beta receptor signaling pathway | 8.16E-14 |
| GO:0045786 | negative regulation of cell cycle | 1.20E-13 |
| GO:0050794 | regulation of cellular process | 1.75E-13 |
| GO:2000113 | negative regulation of cellular macromolecule biosynthetic process | 3.64E-13 |
| GO:0010605 | negative regulation of macromolecule metabolic process | 3.79E-13 |
| GO:0010629 | negative regulation of gene expression | 4.21E-13 |
| GO:0044237 | cellular metabolic process | 4.78E-13 |
| GO:0010558 | negative regulation of macromolecule biosynthetic process | 6.20E-13 |
| GO:0016568 | chromatin modification | 6.47E-13 |
| GO:0048522 | positive regulation of cellular process | 1.03E-12 |
| GO:0009892 | negative regulation of metabolic process | 1.12E-12 |
| GO:0031327 | negative regulation of cellular biosynthetic process | 1.19E-12 |
| GO:0045892 | negative regulation of transcription, DNA-dependent | 1.23E-12 |
| GO:0045944 | positive regulation of transcription from RNA polymerase II promoter | 1.23E-12 |
| GO:0006325 | chromatin organization | 1.37E-12 |
| GO:0009890 | negative regulation of biosynthetic process | 1.54E-12 |
| GO:0050789 | regulation of biological process | 2.20E-12 |
| GO:0051253 | negative regulation of RNA metabolic process | 2.45E-12 |
| GO:0048518 | positive regulation of biological process | 2.97E-12 |
| GO:0031324 | negative regulation of cellular metabolic process | 3.58E-12 |
| GO:0044238 | primary metabolic process | 5.33E-12 |
| GO:0045934 | negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 8.15E-12 |
| GO:0051172 | negative regulation of nitrogen compound metabolic process | 9.56E-12 |
| GO:0000122 | negative regulation of transcription from RNA polymerase II promoter | 1.19E-11 |
| GO:0007178 | transmembrane receptor protein serine/threonine kinase signaling pathway | 1.35E-11 |
| GO:0065007 | biological regulation | 2.09E-11 |
| GO:0048523 | negative regulation of cellular process | 2.49E-11 |
| GO:0051276 | chromosome organization | 7.33E-11 |
| GO:0008152 | metabolic process | 1.91E-10 |
| GO:0000082 | G1/S transition of mitotic cell cycle | 2.54E-10 |
| GO:0048519 | negative regulation of biological process | 2.68E-10 |
| GO:0007167 | enzyme linked receptor protein signaling pathway | 4.68E-09 |
| GO:0006996 | organelle organization | 9.19E-09 |

| | | |
|------------|--|----------|
| GO:0006464 | protein modification process | 1.20E-08 |
| GO:0007050 | cell cycle arrest | 1.73E-08 |
| GO:0043412 | macromolecule modification | 3.10E-08 |
| GO:0051246 | regulation of protein metabolic process | 3.29E-08 |
| GO:0051716 | cellular response to stimulus | 3.77E-08 |
| GO:0008283 | cell proliferation | 4.90E-08 |
| GO:0030522 | intracellular receptor mediated signaling pathway | 5.47E-08 |
| GO:0000083 | regulation of transcription involved in G1/S phase of mitotic cell cycle | 8.41E-08 |
| GO:0030521 | androgen receptor signaling pathway | 2.42E-07 |
| GO:0007166 | cell surface receptor linked signaling pathway | 2.89E-07 |
| GO:0071841 | cellular component organization or biogenesis at cellular level | 4.00E-07 |
| GO:0009987 | cellular process | 4.02E-07 |
| GO:0007165 | signal transduction | 5.20E-07 |
| GO:0007346 | regulation of mitotic cell cycle | 7.09E-07 |
| GO:0032268 | regulation of cellular protein metabolic process | 7.26E-07 |
| GO:0042127 | regulation of cell proliferation | 9.62E-07 |
| GO:0071842 | cellular component organization at cellular level | 1.57E-06 |
| GO:0051301 | cell division | 1.69E-06 |
| GO:0006974 | response to DNA damage stimulus | 1.90E-06 |
| GO:0006793 | phosphorus metabolic process | 1.98E-06 |
| GO:0006796 | phosphate metabolic process | 1.98E-06 |
| GO:0048585 | negative regulation of response to stimulus | 2.12E-06 |
| GO:0009968 | negative regulation of signal transduction | 2.43E-06 |
| GO:0000075 | cell cycle checkpoint | 2.72E-06 |
| GO:0022415 | viral reproductive process | 2.97E-06 |
| GO:0010646 | regulation of cell communication | 3.83E-06 |
| GO:0023057 | negative regulation of signaling | 5.07E-06 |
| GO:0010648 | negative regulation of cell communication | 5.37E-06 |
| GO:0023052 | signaling | 5.83E-06 |
| GO:0071156 | regulation of cell cycle arrest | 7.38E-06 |
| GO:0071840 | cellular component organization or biogenesis | 7.84E-06 |
| GO:0030518 | steroid hormone receptor signaling pathway | 9.22E-06 |
| GO:0017015 | regulation of transforming growth factor beta receptor signaling pathway | 1.17E-05 |
| GO:0044403 | symbiosis, encompassing mutualism through parasitism | 1.48E-05 |
| GO:0044419 | interspecies interaction between organisms | 1.48E-05 |
| GO:0006338 | chromatin remodeling | 1.48E-05 |
| GO:0009966 | regulation of signal transduction | 1.69E-05 |
| GO:0010564 | regulation of cell cycle process | 1.87E-05 |
| GO:0016310 | phosphorylation | 1.96E-05 |
| GO:0050896 | response to stimulus | 2.53E-05 |
| GO:0044267 | cellular protein metabolic process | 2.56E-05 |
| GO:0016043 | cellular component organization | 2.65E-05 |
| GO:0032501 | multicellular organismal process | 4.83E-05 |
| GO:0016032 | viral reproduction | 4.90E-05 |
| GO:0008219 | cell death | 6.12E-05 |
| GO:0016265 | death | 6.18E-05 |

| | | |
|------------|--|----------|
| GO:0031399 | regulation of protein modification process | 6.37E-05 |
| GO:0000077 | DNA damage checkpoint | 7.88E-05 |
| GO:2000602 | regulation of interphase of mitotic cell cycle | 8.42E-05 |
| GO:0031570 | DNA integrity checkpoint | 1.03E-04 |
| GO:0023051 | regulation of signaling | 1.22E-04 |
| GO:0016570 | histone modification | 1.25E-04 |
| GO:0033554 | cellular response to stress | 1.31E-04 |
| GO:0012501 | programmed cell death | 1.41E-04 |
| GO:0016569 | covalent chromatin modification | 1.44E-04 |
| GO:0048583 | regulation of response to stimulus | 2.06E-04 |
| GO:0090092 | regulation of transmembrane receptor protein serine/threonine kinase signaling pathway | 3.19E-04 |
| GO:0007154 | cell communication | 3.33E-04 |
| GO:0000085 | G2 phase of mitotic cell cycle | 3.69E-04 |
| GO:0051319 | G2 phase | 3.69E-04 |
| GO:0019538 | protein metabolic process | 4.99E-04 |
| GO:0022414 | reproductive process | 5.10E-04 |
| GO:0000003 | reproduction | 5.30E-04 |
| GO:0008150 | biological_process | 5.62E-04 |
| GO:0019048 | virus-host interaction | 7.06E-04 |
| GO:0010941 | regulation of cell death | 7.18E-04 |
| GO:0060766 | negative regulation of androgen receptor signaling pathway | 8.06E-04 |
| GO:0032502 | developmental process | 8.71E-04 |
| GO:0006915 | apoptosis | 8.82E-04 |
| GO:0042325 | regulation of phosphorylation | 0.001292 |
| GO:0000084 | S phase of mitotic cell cycle | 0.001534 |
| GO:0051701 | interaction with host | 0.001971 |
| GO:0007275 | multicellular organismal development | 0.00217 |
| GO:0006476 | protein deacetylation | 0.002273 |
| GO:0051320 | S phase | 0.002404 |
| GO:0006468 | protein phosphorylation | 0.002476 |
| GO:0043921 | modulation by host of viral transcription | 0.002491 |
| GO:0052472 | modulation by host of symbiont transcription | 0.002491 |
| GO:0035601 | protein deacylation | 0.002669 |
| GO:0019220 | regulation of phosphate metabolic process | 0.002906 |
| GO:0051174 | regulation of phosphorus metabolic process | 0.002906 |
| GO:0007219 | Notch signaling pathway | 0.003078 |
| GO:0051247 | positive regulation of protein metabolic process | 0.003334 |
| GO:0052312 | modulation of transcription in other organism involved in symbiotic interaction | 0.003344 |
| GO:0065009 | regulation of molecular function | 0.003395 |
| GO:0042981 | regulation of apoptosis | 0.003489 |
| GO:0009057 | macromolecule catabolic process | 0.003774 |
| GO:0060765 | regulation of androgen receptor signaling pathway | 0.00383 |
| GO:0043067 | regulation of programmed cell death | 0.0039 |
| GO:0040008 | regulation of growth | 0.003905 |
| GO:0030308 | negative regulation of cell growth | 0.003985 |

| | | |
|------------|---|----------|
| GO:0045792 | negative regulation of cell size | 0.005504 |
| GO:0033144 | negative regulation of steroid hormone receptor signaling pathway | 0.00559 |
| GO:0071930 | negative regulation of transcription involved in G1/S phase of mitotic cell cycle | 0.006098 |
| GO:0006259 | DNA metabolic process | 0.006189 |
| GO:0030511 | positive regulation of transforming growth factor beta receptor signaling pathway | 0.006265 |
| GO:0051851 | modification by host of symbiont morphology or physiology | 0.006265 |
| GO:0006950 | response to stress | 0.007422 |
| GO:0051702 | interaction with symbiont | 0.010562 |
| GO:0030163 | protein catabolic process | 0.011602 |
| GO:0040007 | growth | 0.011626 |
| GO:0072131 | kidney mesenchyme morphogenesis | 0.012105 |
| GO:0072133 | metanephric mesenchyme morphogenesis | 0.012105 |
| GO:2000045 | regulation of G1/S transition of mitotic cell cycle | 0.012532 |
| GO:0060070 | canonical Wnt receptor signaling pathway | 0.012542 |
| GO:0048011 | nerve growth factor receptor signaling pathway | 0.013046 |
| GO:0016458 | gene silencing | 0.013426 |
| GO:0042176 | regulation of protein catabolic process | 0.013827 |
| GO:0032270 | positive regulation of cellular protein metabolic process | 0.013945 |
| GO:0000280 | nuclear division | 0.016573 |
| GO:0007067 | mitosis | 0.016573 |
| GO:0070887 | cellular response to chemical stimulus | 0.016803 |
| GO:0000279 | M phase | 0.017864 |
| GO:0033044 | regulation of chromosome organization | 0.018696 |
| GO:0051248 | negative regulation of protein metabolic process | 0.019945 |
| GO:0006260 | DNA replication | 0.020179 |
| GO:0031572 | G2/M transition DNA damage checkpoint | 0.020654 |
| GO:0000087 | M phase of mitotic cell cycle | 0.020655 |
| GO:0016055 | Wnt receptor signaling pathway | 0.021412 |
| GO:0000079 | regulation of cyclin-dependent protein kinase activity | 0.021785 |
| GO:0048285 | organelle fission | 0.024695 |
| GO:0030330 | DNA damage response, signal transduction by p53 class mediator | 0.027625 |
| GO:0045926 | negative regulation of growth | 0.029734 |
| GO:0072331 | signal transduction by p53 class mediator | 0.031797 |
| GO:0006270 | DNA-dependent DNA replication initiation | 0.033544 |
| GO:0051128 | regulation of cellular component organization | 0.037366 |
| GO:0033143 | regulation of steroid hormone receptor signaling pathway | 0.040376 |
| GO:0045930 | negative regulation of mitotic cell cycle | 0.040376 |
| GO:0016575 | histone deacetylation | 0.042813 |
| GO:0031576 | G2/M transition checkpoint | 0.04537 |
| GO:0000086 | G2/M transition of mitotic cell cycle | 0.049424 |
| GO:0007093 | mitotic cell cycle checkpoint | 0.055716 |
| GO:0008285 | negative regulation of cell proliferation | 0.057327 |
| GO:0060828 | regulation of canonical Wnt receptor signaling pathway | 0.058359 |
| GO:0001932 | regulation of protein phosphorylation | 0.059492 |
| GO:0008361 | regulation of cell size | 0.063043 |
| GO:0051704 | multi-organism process | 0.063097 |

| | | |
|------------|---|----------|
| GO:0042770 | signal transduction in response to DNA damage | 0.074854 |
| GO:0048513 | organ development | 0.081006 |
| GO:0048856 | anatomical structure development | 0.087414 |
| GO:0009967 | positive regulation of signal transduction | 0.087466 |
| GO:0043549 | regulation of kinase activity | 0.087466 |
| GO:0040016 | embryonic cleavage | 0.087762 |
| GO:0051571 | positive regulation of histone H3-K4 methylation | 0.087762 |
| GO:0060548 | negative regulation of cell death | 0.089071 |
| GO:0050790 | regulation of catalytic activity | 0.091505 |
| GO:0090068 | positive regulation of cell cycle process | 0.097981 |
| GO:0051338 | regulation of transferase activity | 0.103687 |
| GO:0046782 | regulation of viral transcription | 0.104488 |
| GO:0007183 | SMAD protein complex assembly | 0.106449 |
| GO:0010870 | positive regulation of receptor biosynthetic process | 0.106449 |
| GO:0032906 | transforming growth factor-beta2 production | 0.106449 |
| GO:0032909 | regulation of transforming growth factor-beta2 production | 0.106449 |
| GO:0043923 | positive regulation by host of viral transcription | 0.106449 |
| GO:0035821 | modification of morphology or physiology of other organism | 0.108532 |
| GO:0051817 | modification of morphology or physiology of other organism involved in symbiotic interaction | 0.108532 |
| GO:0010647 | positive regulation of cell communication | 0.132597 |
| GO:0023056 | positive regulation of signaling | 0.134267 |
| GO:0031396 | regulation of protein ubiquitination | 0.145406 |
| GO:0030512 | negative regulation of transforming growth factor beta receptor signaling pathway | 0.154696 |
| GO:0009887 | organ morphogenesis | 0.154895 |
| GO:0000216 | M/G1 transition of mitotic cell cycle | 0.16029 |
| GO:0048524 | positive regulation of viral reproduction | 0.16029 |
| GO:0051222 | positive regulation of protein transport | 0.164463 |
| GO:0001558 | regulation of cell growth | 0.166703 |
| GO:0051130 | positive regulation of cellular component organization | 0.167771 |
| GO:0042221 | response to chemical stimulus | 0.169219 |
| GO:0032446 | protein modification by small protein conjugation | 0.170271 |
| GO:0031062 | positive regulation of histone methylation | 0.199444 |
| GO:0072075 | metanephric mesenchyme development | 0.199444 |
| GO:0071158 | positive regulation of cell cycle arrest | 0.204343 |
| GO:0090100 | positive regulation of transmembrane receptor protein serine/threonine kinase signaling pathway | 0.211253 |
| GO:0030154 | cell differentiation | 0.212624 |
| GO:0046824 | positive regulation of nucleocytoplasmic transport | 0.21817 |
| GO:0032535 | regulation of cellular component size | 0.22414 |
| GO:0001756 | somitogenesis | 0.225226 |
| GO:0061197 | fungiform papilla morphogenesis | 0.226604 |
| GO:0061198 | fungiform papilla formation | 0.226604 |
| GO:0009894 | regulation of catabolic process | 0.235671 |
| GO:0031575 | mitotic cell cycle G1/S transition checkpoint | 0.239757 |
| GO:0031400 | negative regulation of protein modification process | 0.243023 |
| GO:0048145 | regulation of fibroblast proliferation | 0.247234 |

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|------------|---|----------|
| GO:0030111 | regulation of Wnt receptor signaling pathway | 0.254473 |
| GO:0045862 | positive regulation of proteolysis | 0.254689 |
| GO:0071779 | G1/S transition checkpoint | 0.254689 |
| GO:0048731 | system development | 0.257457 |
| GO:0019058 | viral infectious cycle | 0.261862 |
| GO:0048144 | fibroblast proliferation | 0.270525 |
| GO:0001654 | eye development | 0.282447 |
| GO:0010869 | regulation of receptor biosynthetic process | 0.285904 |
| GO:0061196 | fungiform papilla development | 0.285904 |
| GO:0072074 | kidney mesenchyme development | 0.285904 |
| GO:0051094 | positive regulation of developmental process | 0.294522 |
| GO:0070647 | protein modification by small protein conjugation or removal | 0.294935 |
| GO:0010720 | positive regulation of cell development | 0.30331 |
| GO:0061053 | somite development | 0.303612 |
| GO:0045749 | negative regulation of S phase of mitotic cell cycle | 0.31765 |
| GO:0051569 | regulation of histone H3-K4 methylation | 0.31765 |
| GO:0061029 | eyelid development in camera-type eye | 0.31765 |
| GO:0032880 | regulation of protein localization | 0.342782 |
| GO:0060789 | hair follicle placode formation | 0.352001 |
| GO:0009790 | embryo development | 0.353655 |
| GO:0071900 | regulation of protein serine/threonine kinase activity | 0.358184 |
| GO:0050792 | regulation of viral reproduction | 0.388589 |
| GO:0090316 | positive regulation of intracellular protein transport | 0.388589 |
| GO:0048869 | cellular developmental process | 0.38877 |
| GO:0045597 | positive regulation of cell differentiation | 0.390617 |
| GO:0048584 | positive regulation of response to stimulus | 0.395905 |
| GO:0090101 | negative regulation of transmembrane receptor protein serine/threonine kinase signaling pathway | 0.419781 |
| GO:0045732 | positive regulation of protein catabolic process | 0.441897 |
| GO:0010638 | positive regulation of organelle organization | 0.450629 |
| GO:0010718 | positive regulation of epithelial to mesenchymal transition | 0.463515 |
| GO:0032388 | positive regulation of intracellular transport | 0.463515 |
| GO:0072132 | mesenchyme morphogenesis | 0.463515 |
| GO:0000226 | microtubule cytoskeleton organization | 0.46883 |
| GO:0043161 | proteasomal ubiquitin-dependent protein catabolic process | 0.479148 |
| GO:0050678 | regulation of epithelial cell proliferation | 0.479148 |
| GO:0016049 | cell growth | 0.484025 |
| GO:0043066 | negative regulation of apoptosis | 0.484025 |
| GO:0032800 | receptor biosynthetic process | 0.503187 |
| GO:0043069 | negative regulation of programmed cell death | 0.521678 |
| GO:0090066 | regulation of anatomical structure size | 0.534248 |
| GO:0010498 | proteasomal protein catabolic process | 0.535315 |
| GO:0045859 | regulation of protein kinase activity | 0.540259 |
| GO:0035412 | regulation of catenin import into nucleus | 0.585784 |
| GO:0043587 | tongue morphogenesis | 0.585784 |
| GO:0035282 | segmentation | 0.595619 |

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| GO:0001942 | hair follicle development | 0.636397 |
| GO:0022404 | molting cycle process | 0.636397 |
| GO:0022405 | hair cycle process | 0.636397 |
| GO:0010770 | positive regulation of cell morphogenesis involved in differentiation | 0.677145 |
| GO:0035411 | catenin import into nucleus | 0.677145 |
| GO:0070303 | negative regulation of stress-activated protein kinase signaling cascade | 0.677145 |
| GO:0010033 | response to organic substance | 0.715689 |
| GO:0031060 | regulation of histone methylation | 0.725805 |
| GO:0042303 | molting cycle | 0.738143 |
| GO:0042633 | hair cycle | 0.738143 |
| GO:0010948 | negative regulation of cell cycle process | 0.753444 |
| GO:0006261 | DNA-dependent DNA replication | 0.768939 |
| GO:0051054 | positive regulation of DNA metabolic process | 0.784629 |
| GO:0050673 | epithelial cell proliferation | 0.80603 |
| GO:0071359 | cellular response to dsRNA | 0.825613 |
| GO:0008284 | positive regulation of cell proliferation | 0.862046 |
| GO:0080134 | regulation of response to stress | 0.881011 |
| GO:0048147 | negative regulation of fibroblast proliferation | 0.931052 |
| GO:0071604 | transforming growth factor-beta production | 0.931052 |
| GO:0071634 | regulation of transforming growth factor-beta production | 0.931052 |
| GO:0007090 | regulation of S phase of mitotic cell cycle | 0.986514 |
| GO:0016925 | protein sumoylation | 0.986514 |
| GO:0051568 | histone H3-K4 methylation | 0.986514 |

Cellular Component

| GO id | GO name | adjusted-P |
|------------|--|------------|
| GO:0005654 | nucleoplasm | 3.40E-33 |
| GO:0031981 | nuclear lumen | 4.89E-33 |
| GO:0070013 | intracellular organelle lumen | 1.84E-31 |
| GO:0044428 | nuclear part | 2.34E-31 |
| GO:0043233 | organelle lumen | 3.08E-31 |
| GO:0031974 | membrane-enclosed lumen | 5.82E-31 |
| GO:0005634 | nucleus | 5.13E-22 |
| GO:0044446 | intracellular organelle part | 2.25E-19 |
| GO:0044422 | organelle part | 4.63E-19 |
| GO:0044451 | nucleoplasm part | 3.69E-18 |
| GO:0043231 | intracellular membrane-bounded organelle | 2.12E-14 |
| GO:0043227 | membrane-bounded organelle | 2.45E-14 |
| GO:0005667 | transcription factor complex | 2.70E-14 |
| GO:0043234 | protein complex | 4.11E-14 |
| GO:0043229 | intracellular organelle | 5.00E-13 |
| GO:0044424 | intracellular part | 5.66E-13 |
| GO:0043226 | organelle | 5.74E-13 |
| GO:0032991 | macromolecular complex | 5.24E-12 |

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|------------|--|----------|
| GO:0005622 | intracellular | 9.43E-11 |
| GO:0005694 | chromosome | 4.30E-09 |
| GO:0044427 | chromosomal part | 7.72E-09 |
| GO:0000785 | chromatin | 4.48E-06 |
| GO:0043228 | non-membrane-bounded organelle | 6.27E-06 |
| GO:0043232 | intracellular non-membrane-bounded organelle | 6.27E-06 |
| GO:0071141 | SMAD protein complex | 2.29E-05 |
| GO:0016585 | chromatin remodeling complex | 5.57E-05 |
| GO:0044464 | cell part | 7.75E-05 |
| GO:0005623 | cell | 7.75E-05 |
| GO:0017053 | transcriptional repressor complex | 1.25E-04 |
| GO:0005575 | cellular_component | 0.001381 |
| GO:0015630 | microtubule cytoskeleton | 0.005516 |
| GO:0035189 | Rb-E2F complex | 0.012105 |
| GO:0000228 | nuclear chromosome | 0.019712 |
| GO:0000118 | histone deacetylase complex | 0.087762 |
| GO:0035097 | histone methyltransferase complex | 0.104488 |
| GO:0034708 | methyltransferase complex | 0.122868 |
| GO:0016580 | Sin3 complex | 0.127003 |
| GO:0070822 | Sin3-type complex | 0.127003 |
| GO:0044454 | nuclear chromosome part | 0.14449 |
| GO:0016514 | SWI/SNF complex | 0.352001 |
| GO:0005819 | spindle | 0.554758 |
| GO:0000307 | cyclin-dependent protein kinase holoenzyme complex | 0.585784 |
| GO:0016581 | NuRD complex | 0.585784 |
| GO:0044430 | cytoskeletal part | 0.80603 |
| GO:0005730 | nucleolus | 0.89529 |

Molecular Function

| GO id | GO name | adjusted-P |
|------------|---|------------|
| GO:0005515 | protein binding | 1.78E-17 |
| GO:0008134 | transcription factor binding | 4.20E-16 |
| GO:0000988 | protein binding transcription factor activity | 7.21E-14 |
| GO:0003677 | DNA binding | 3.95E-12 |
| GO:0003712 | transcription cofactor activity | 2.74E-11 |
| GO:0000989 | transcription factor binding transcription factor activity | 3.69E-11 |
| GO:0003700 | sequence-specific DNA binding transcription factor activity | 3.50E-09 |
| GO:0001071 | nucleic acid binding transcription factor activity | 3.65E-09 |
| GO:0044212 | transcription regulatory region DNA binding | 9.43E-09 |
| GO:0000975 | regulatory region DNA binding | 2.12E-08 |
| GO:0001067 | regulatory region nucleic acid binding | 2.12E-08 |
| GO:0003676 | nucleic acid binding | 4.54E-07 |
| GO:0005488 | binding | 1.04E-06 |
| GO:0019899 | enzyme binding | 2.25E-05 |

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|------------|--|----------|
| GO:0003682 | chromatin binding | 3.89E-05 |
| GO:0003714 | transcription corepressor activity | 5.73E-05 |
| GO:0003713 | transcription coactivator activity | 1.15E-04 |
| GO:0001085 | RNA polymerase II transcription factor binding | 1.97E-04 |
| GO:0050681 | androgen receptor binding | 3.12E-04 |
| GO:0031078 | histone deacetylase activity (H3-K14 specific) | 4.91E-04 |
| GO:0032041 | NAD-dependent histone deacetylase activity (H3-K14 specific) | 4.91E-04 |
| GO:0046970 | NAD-dependent histone deacetylase activity (H4-K16 specific) | 4.91E-04 |
| GO:0032129 | histone deacetylase activity (H3-K9 specific) | 8.06E-04 |
| GO:0046969 | NAD-dependent histone deacetylase activity (H3-K9 specific) | 8.06E-04 |
| GO:0017136 | NAD-dependent histone deacetylase activity | 0.001236 |
| GO:0034979 | NAD-dependent protein deacetylase activity | 0.001236 |
| GO:0070491 | repressing transcription factor binding | 0.001704 |
| GO:0035257 | nuclear hormone receptor binding | 0.002612 |
| GO:0035258 | steroid hormone receptor binding | 0.003117 |
| GO:0001047 | core promoter binding | 0.003616 |
| GO:0051427 | hormone receptor binding | 0.006043 |
| GO:0001103 | RNA polymerase II repressing transcription factor binding | 0.007007 |
| GO:0004407 | histone deacetylase activity | 0.042813 |
| GO:0033613 | activating transcription factor binding | 0.050778 |
| GO:0033558 | protein deacetylase activity | 0.053632 |
| GO:0031490 | chromatin DNA binding | 0.08027 |
| GO:0005072 | transforming growth factor beta receptor, cytoplasmic mediator activity | 0.087762 |
| GO:0031625 | ubiquitin protein ligase binding | 0.107799 |
| GO:0019213 | deacetylase activity | 0.113159 |
| GO:0019900 | kinase binding | 0.125487 |
| GO:0042826 | histone deacetylase binding | 0.178148 |
| GO:0070577 | histone acetyl-lysine binding | 0.199444 |
| GO:0046332 | SMAD binding | 0.312456 |
| GO:0003674 | molecular_function | 0.450629 |
| GO:0001104 | RNA polymerase II transcription cofactor activity | 0.534248 |
| GO:0017025 | TBP-class protein binding | 0.544375 |
| GO:0019901 | protein kinase binding | 0.57412 |
| GO:0001106 | RNA polymerase II transcription corepressor activity | 0.585784 |
| GO:0016538 | cyclin-dependent protein kinase regulator activity | 0.585784 |
| GO:0070412 | R-SMAD binding | 0.585784 |
| GO:0001076 | RNA polymerase II transcription factor binding transcription factor activity | 0.917872 |
| GO:0001102 | RNA polymerase II activating transcription factor binding | 0.931052 |

Table S17. GO term enrichment of human p130 interactors**Biological Process**

| GO id | GO name | adjusted-P |
|--------------|---|-------------------|
| GO:0000278 | mitotic cell cycle | 8.55E-33 |
| GO:0007049 | cell cycle | 6.36E-31 |
| GO:0051329 | interphase of mitotic cell cycle | 5.36E-27 |
| GO:0051325 | interphase | 7.66E-27 |
| GO:0060255 | regulation of macromolecule metabolic process | 8.04E-22 |
| GO:0022402 | cell cycle process | 1.34E-21 |
| GO:0080090 | regulation of primary metabolic process | 2.55E-21 |
| GO:0031323 | regulation of cellular metabolic process | 3.97E-21 |
| GO:0019222 | regulation of metabolic process | 4.13E-21 |
| GO:0022403 | cell cycle phase | 4.25E-21 |
| GO:0000080 | G1 phase of mitotic cell cycle | 6.54E-21 |
| GO:0051318 | G1 phase | 1.09E-20 |
| GO:0000082 | G1/S transition of mitotic cell cycle | 2.01E-18 |
| GO:0051252 | regulation of RNA metabolic process | 4.17E-18 |
| GO:0031326 | regulation of cellular biosynthetic process | 5.88E-18 |
| GO:0010468 | regulation of gene expression | 6.59E-18 |
| GO:0009889 | regulation of biosynthetic process | 7.46E-18 |
| GO:0034645 | cellular macromolecule biosynthetic process | 7.95E-18 |
| GO:0019219 | regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 1.06E-17 |
| GO:0009059 | macromolecule biosynthetic process | 1.58E-17 |
| GO:2000112 | regulation of cellular macromolecule biosynthetic process | 1.64E-17 |
| GO:0051171 | regulation of nitrogen compound metabolic process | 1.77E-17 |
| GO:0010556 | regulation of macromolecule biosynthetic process | 2.71E-17 |
| GO:0006355 | regulation of transcription, DNA-dependent | 3.84E-17 |
| GO:0090304 | nucleic acid metabolic process | 6.07E-17 |
| GO:0006351 | transcription, DNA-dependent | 8.95E-17 |
| GO:0051726 | regulation of cell cycle | 9.41E-17 |
| GO:0044260 | cellular macromolecule metabolic process | 1.18E-16 |
| GO:0010604 | positive regulation of macromolecule metabolic process | 1.21E-16 |
| GO:0031325 | positive regulation of cellular metabolic process | 1.31E-16 |
| GO:0032774 | RNA biosynthetic process | 1.47E-16 |
| GO:0009893 | positive regulation of metabolic process | 6.03E-16 |
| GO:0006139 | nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 8.93E-16 |
| GO:0044249 | cellular biosynthetic process | 9.90E-16 |
| GO:0043170 | macromolecule metabolic process | 1.00E-15 |
| GO:0010557 | positive regulation of macromolecule biosynthetic process | 1.55E-15 |
| GO:0016070 | RNA metabolic process | 2.48E-15 |
| GO:0009058 | biosynthetic process | 2.61E-15 |
| GO:0006366 | transcription from RNA polymerase II promoter | 3.23E-15 |

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|------------|--|----------|
| GO:0045893 | positive regulation of transcription, DNA-dependent | 3.68E-15 |
| GO:0031328 | positive regulation of cellular biosynthetic process | 5.59E-15 |
| GO:0006357 | regulation of transcription from RNA polymerase II promoter | 5.72E-15 |
| GO:0051254 | positive regulation of RNA metabolic process | 7.13E-15 |
| GO:0009891 | positive regulation of biosynthetic process | 7.30E-15 |
| GO:0010467 | gene expression | 1.04E-14 |
| GO:0010628 | positive regulation of gene expression | 1.72E-14 |
| GO:0034641 | cellular nitrogen compound metabolic process | 2.01E-14 |
| GO:0050794 | regulation of cellular process | 2.49E-14 |
| GO:0045935 | positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 3.23E-14 |
| GO:0051173 | positive regulation of nitrogen compound metabolic process | 4.54E-14 |
| GO:0006807 | nitrogen compound metabolic process | 5.46E-14 |
| GO:0016568 | chromatin modification | 8.00E-14 |
| GO:0048522 | positive regulation of cellular process | 1.27E-13 |
| GO:0006325 | chromatin organization | 1.44E-13 |
| GO:0050789 | regulation of biological process | 2.81E-13 |
| GO:0045786 | negative regulation of cell cycle | 4.82E-13 |
| GO:0065007 | biological regulation | 2.44E-12 |
| GO:0048518 | positive regulation of biological process | 3.64E-12 |
| GO:0044238 | primary metabolic process | 4.47E-12 |
| GO:0048523 | negative regulation of cellular process | 4.78E-12 |
| GO:0051276 | chromosome organization | 7.98E-12 |
| GO:0044237 | cellular metabolic process | 9.42E-12 |
| GO:0051246 | regulation of protein metabolic process | 1.18E-11 |
| GO:0048519 | negative regulation of biological process | 4.89E-11 |
| GO:0045944 | positive regulation of transcription from RNA polymerase II promoter | 5.67E-11 |
| GO:0000084 | S phase of mitotic cell cycle | 6.67E-11 |
| GO:0010605 | negative regulation of macromolecule metabolic process | 8.65E-11 |
| GO:0007050 | cell cycle arrest | 1.12E-10 |
| GO:0008152 | metabolic process | 1.26E-10 |
| GO:0051320 | S phase | 1.54E-10 |
| GO:0009892 | negative regulation of metabolic process | 2.19E-10 |
| GO:0030522 | intracellular receptor mediated signaling pathway | 3.33E-10 |
| GO:0032268 | regulation of cellular protein metabolic process | 4.21E-10 |
| GO:0006352 | transcription initiation, DNA-dependent | 6.53E-10 |
| GO:0031324 | negative regulation of cellular metabolic process | 8.50E-10 |
| GO:0051716 | cellular response to stimulus | 1.97E-09 |
| GO:0006367 | transcription initiation from RNA polymerase II promoter | 2.06E-09 |
| GO:2000113 | negative regulation of cellular macromolecule biosynthetic process | 3.20E-09 |
| GO:0010629 | negative regulation of gene expression | 3.58E-09 |
| GO:0031399 | regulation of protein modification process | 4.61E-09 |
| GO:0010558 | negative regulation of macromolecule biosynthetic process | 4.85E-09 |
| GO:0031327 | negative regulation of cellular biosynthetic process | 8.08E-09 |
| GO:0009890 | negative regulation of biosynthetic process | 9.88E-09 |
| GO:0045892 | negative regulation of transcription, DNA-dependent | 1.35E-08 |

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|------------|--|----------|
| GO:0009987 | cellular process | 1.55E-08 |
| GO:0051253 | negative regulation of RNA metabolic process | 2.30E-08 |
| GO:0022415 | viral reproductive process | 3.18E-08 |
| GO:0016032 | viral reproduction | 3.85E-08 |
| GO:0000083 | regulation of transcription involved in G1/S phase of mitotic cell cycle | 4.07E-08 |
| GO:0006996 | organelle organization | 4.90E-08 |
| GO:0030518 | steroid hormone receptor signaling pathway | 5.61E-08 |
| GO:0045934 | negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 5.80E-08 |
| GO:0051172 | negative regulation of nitrogen compound metabolic process | 6.55E-08 |
| GO:0007165 | signal transduction | 6.78E-08 |
| GO:0071156 | regulation of cell cycle arrest | 7.22E-08 |
| GO:0030521 | androgen receptor signaling pathway | 1.02E-07 |
| GO:0007179 | transforming growth factor beta receptor signaling pathway | 1.54E-07 |
| GO:0050896 | response to stimulus | 1.57E-07 |
| GO:0044403 | symbiosis, encompassing mutualism through parasitism | 1.78E-07 |
| GO:0044419 | interspecies interaction between organisms | 1.78E-07 |
| GO:0010564 | regulation of cell cycle process | 2.32E-07 |
| GO:0000122 | negative regulation of transcription from RNA polymerase II promoter | 4.06E-07 |
| GO:0006464 | protein modification process | 4.50E-07 |
| GO:0008283 | cell proliferation | 4.84E-07 |
| GO:0023052 | signaling | 7.55E-07 |
| GO:2000602 | regulation of interphase of mitotic cell cycle | 7.63E-07 |
| GO:0000075 | cell cycle checkpoint | 8.73E-07 |
| GO:0043412 | macromolecule modification | 1.02E-06 |
| GO:0007166 | cell surface receptor linked signaling pathway | 1.42E-06 |
| GO:0071840 | cellular component organization or biogenesis | 1.50E-06 |
| GO:0016570 | histone modification | 1.56E-06 |
| GO:0016569 | covalent chromatin modification | 1.84E-06 |
| GO:0016310 | phosphorylation | 2.87E-06 |
| GO:0007178 | transmembrane receptor protein serine/threonine kinase signaling pathway | 4.43E-06 |
| GO:0006974 | response to DNA damage stimulus | 5.51E-06 |
| GO:0071841 | cellular component organization or biogenesis at cellular level | 5.63E-06 |
| GO:0007346 | regulation of mitotic cell cycle | 5.80E-06 |
| GO:0016043 | cellular component organization | 6.06E-06 |
| GO:0006338 | chromatin remodeling | 6.27E-06 |
| GO:0065009 | regulation of molecular function | 9.51E-06 |
| GO:0022414 | reproductive process | 9.81E-06 |
| GO:0000003 | reproduction | 1.02E-05 |
| GO:0019048 | virus-host interaction | 1.17E-05 |
| GO:0042127 | regulation of cell proliferation | 1.55E-05 |
| GO:0008150 | biological_process | 1.86E-05 |
| GO:0006793 | phosphorus metabolic process | 2.18E-05 |
| GO:0006796 | phosphate metabolic process | 2.18E-05 |
| GO:0033554 | cellular response to stress | 2.28E-05 |
| GO:0071842 | cellular component organization at cellular level | 2.34E-05 |

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|------------|--|----------|
| GO:0006260 | DNA replication | 2.44E-05 |
| GO:0042325 | regulation of phosphorylation | 2.93E-05 |
| GO:0007167 | enzyme linked receptor protein signaling pathway | 3.01E-05 |
| GO:0000077 | DNA damage checkpoint | 3.36E-05 |
| GO:0051701 | interaction with host | 3.84E-05 |
| GO:0007219 | Notch signaling pathway | 3.97E-05 |
| GO:0031570 | DNA integrity checkpoint | 4.37E-05 |
| GO:0044267 | cellular protein metabolic process | 5.48E-05 |
| GO:0050790 | regulation of catalytic activity | 5.59E-05 |
| GO:0031145 | anaphase-promoting complex-dependent proteasomal ubiquitin-dependent protein catabolic process | 6.09E-05 |
| GO:0019220 | regulation of phosphate metabolic process | 7.34E-05 |
| GO:0051174 | regulation of phosphorus metabolic process | 7.34E-05 |
| GO:0031396 | regulation of protein ubiquitination | 9.84E-05 |
| GO:0019538 | protein metabolic process | 1.33E-04 |
| GO:2000045 | regulation of G1/S transition of mitotic cell cycle | 1.40E-04 |
| GO:0051301 | cell division | 1.66E-04 |
| GO:0006259 | DNA metabolic process | 1.74E-04 |
| GO:0012501 | programmed cell death | 1.89E-04 |
| GO:0043549 | regulation of kinase activity | 2.68E-04 |
| GO:0033143 | regulation of steroid hormone receptor signaling pathway | 2.92E-04 |
| GO:0051338 | regulation of transferase activity | 3.39E-04 |
| GO:0032270 | positive regulation of cellular protein metabolic process | 3.82E-04 |
| GO:0030330 | DNA damage response, signal transduction by p53 class mediator | 3.83E-04 |
| GO:0072331 | signal transduction by p53 class mediator | 4.58E-04 |
| GO:0060766 | negative regulation of androgen receptor signaling pathway | 5.13E-04 |
| GO:0008219 | cell death | 5.60E-04 |
| GO:0016265 | death | 5.65E-04 |
| GO:0006468 | protein phosphorylation | 5.88E-04 |
| GO:0043161 | proteasomal ubiquitin-dependent protein catabolic process | 6.49E-04 |
| GO:0010498 | proteasomal protein catabolic process | 7.75E-04 |
| GO:0000086 | G2/M transition of mitotic cell cycle | 8.01E-04 |
| GO:0042981 | regulation of apoptosis | 8.38E-04 |
| GO:0007093 | mitotic cell cycle checkpoint | 9.34E-04 |
| GO:0043067 | regulation of programmed cell death | 9.40E-04 |
| GO:0032501 | multicellular organismal process | 0.001015 |
| GO:0051247 | positive regulation of protein metabolic process | 0.001139 |
| GO:0044265 | cellular macromolecule catabolic process | 0.001171 |
| GO:0006915 | apoptosis | 0.001284 |
| GO:0010941 | regulation of cell death | 0.0013 |
| GO:0042770 | signal transduction in response to DNA damage | 0.001356 |
| GO:0043921 | modulation by host of viral transcription | 0.00158 |
| GO:0052472 | modulation by host of symbiont transcription | 0.00158 |
| GO:0051439 | regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle | 0.001739 |
| GO:0007154 | cell communication | 0.00191 |
| GO:0090068 | positive regulation of cell cycle process | 0.001917 |

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|------------|---|----------|
| GO:0052312 | modulation of transcription in other organism involved in symbiotic interaction | 0.002124 |
| GO:0001932 | regulation of protein phosphorylation | 0.00225 |
| GO:0060765 | regulation of androgen receptor signaling pathway | 0.002438 |
| GO:0045859 | regulation of protein kinase activity | 0.002477 |
| GO:0051704 | multi-organism process | 0.002486 |
| GO:0071158 | positive regulation of cell cycle arrest | 0.002683 |
| GO:0031575 | mitotic cell cycle G1/S transition checkpoint | 0.003351 |
| GO:0033144 | negative regulation of steroid hormone receptor signaling pathway | 0.003558 |
| GO:0010646 | regulation of cell communication | 0.003578 |
| GO:0071779 | G1/S transition checkpoint | 0.003645 |
| GO:0051851 | modification by host of symbiont morphology or physiology | 0.003989 |
| GO:0030163 | protein catabolic process | 0.004016 |
| GO:0016567 | protein ubiquitination | 0.004374 |
| GO:0006950 | response to stress | 0.004842 |
| GO:0051438 | regulation of ubiquitin-protein ligase activity | 0.005025 |
| GO:0032502 | developmental process | 0.005503 |
| GO:0051340 | regulation of ligase activity | 0.005849 |
| GO:0006511 | ubiquitin-dependent protein catabolic process | 0.005892 |
| GO:0048583 | regulation of response to stimulus | 0.005929 |
| GO:0019941 | modification-dependent protein catabolic process | 0.0063 |
| GO:0043632 | modification-dependent macromolecule catabolic process | 0.006482 |
| GO:0032446 | protein modification by small protein conjugation | 0.006604 |
| GO:0051702 | interaction with symbiont | 0.006681 |
| GO:0009966 | regulation of signal transduction | 0.007044 |
| GO:0009057 | macromolecule catabolic process | 0.009202 |
| GO:0051603 | proteolysis involved in cellular protein catabolic process | 0.010176 |
| GO:0048585 | negative regulation of response to stimulus | 0.010446 |
| GO:0044257 | cellular protein catabolic process | 0.011803 |
| GO:0070647 | protein modification by small protein conjugation or removal | 0.012974 |
| GO:0031572 | G2/M transition DNA damage checkpoint | 0.013148 |
| GO:0045605 | negative regulation of epidermal cell differentiation | 0.014475 |
| GO:0007275 | multicellular organismal development | 0.017408 |
| GO:0031401 | positive regulation of protein modification process | 0.020615 |
| GO:0006270 | DNA-dependent DNA replication initiation | 0.021405 |
| GO:0009968 | negative regulation of signal transduction | 0.021507 |
| GO:0031398 | positive regulation of protein ubiquitination | 0.024616 |
| GO:0031576 | G2/M transition checkpoint | 0.029016 |
| GO:0070887 | cellular response to chemical stimulus | 0.029025 |
| GO:0023051 | regulation of signaling | 0.029389 |
| GO:0023057 | negative regulation of signaling | 0.033775 |
| GO:0055123 | digestive system development | 0.03457 |
| GO:0010648 | negative regulation of cell communication | 0.034955 |
| GO:0045683 | negative regulation of epidermis development | 0.040083 |
| GO:0034968 | histone lysine methylation | 0.042254 |
| GO:0008630 | DNA damage response, signal transduction resulting in induction of apoptosis | 0.05386 |

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| GO:0030308 | negative regulation of cell growth | 0.056964 |
| GO:0040016 | embryonic cleavage | 0.063955 |
| GO:0045651 | positive regulation of macrophage differentiation | 0.063955 |
| GO:0051571 | positive regulation of histone H3-K4 methylation | 0.063955 |
| GO:0046782 | regulation of viral transcription | 0.067185 |
| GO:0006917 | induction of apoptosis | 0.068065 |
| GO:0035821 | modification of morphology or physiology of other organism | 0.070005 |
| GO:0051817 | modification of morphology or physiology of other organism involved in symbiotic interaction | 0.070005 |
| GO:0012502 | induction of programmed cell death | 0.072053 |
| GO:0045792 | negative regulation of cell size | 0.073155 |
| GO:0048513 | organ development | 0.075235 |
| GO:0051437 | positive regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle | 0.075964 |
| GO:0043923 | positive regulation by host of viral transcription | 0.0776 |
| GO:0007126 | meiosis | 0.080081 |
| GO:0051327 | M phase of meiotic cell cycle | 0.080081 |
| GO:0000279 | M phase | 0.081773 |
| GO:0051321 | meiotic cell cycle | 0.090925 |
| GO:0000216 | M/G1 transition of mitotic cell cycle | 0.103169 |
| GO:0031571 | mitotic cell cycle G1/S transition DNA damage checkpoint | 0.103169 |
| GO:0048524 | positive regulation of viral reproduction | 0.103169 |
| GO:0000280 | nuclear division | 0.109864 |
| GO:0007067 | mitosis | 0.109864 |
| GO:0065008 | regulation of biological quality | 0.113572 |
| GO:0051443 | positive regulation of ubiquitin-protein ligase activity | 0.114673 |
| GO:0048468 | cell development | 0.120304 |
| GO:0006978 | DNA damage response, signal transduction by p53 class mediator resulting in transcription of p21 class mediator | 0.126437 |
| GO:0016571 | histone methylation | 0.127204 |
| GO:0051248 | negative regulation of protein metabolic process | 0.127847 |
| GO:0008629 | induction of apoptosis by intracellular signals | 0.131388 |
| GO:0051351 | positive regulation of ligase activity | 0.131388 |
| GO:0000087 | M phase of mitotic cell cycle | 0.131552 |
| GO:0031400 | negative regulation of protein modification process | 0.139341 |
| GO:0048011 | nerve growth factor receptor signaling pathway | 0.143751 |
| GO:0031062 | positive regulation of histone methylation | 0.144808 |
| GO:0042772 | DNA damage response, signal transduction resulting in transcription | 0.144808 |
| GO:0071824 | protein-DNA complex subunit organization | 0.147956 |
| GO:0019058 | viral infectious cycle | 0.150191 |
| GO:0048285 | organelle fission | 0.151991 |
| GO:0044248 | cellular catabolic process | 0.159963 |
| GO:0048856 | anatomical structure development | 0.177796 |
| GO:0045595 | regulation of cell differentiation | 0.181914 |
| GO:0071900 | regulation of protein serine/threonine kinase activity | 0.185154 |
| GO:0030154 | cell differentiation | 0.187965 |
| GO:0044085 | cellular component biogenesis | 0.205437 |

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| GO:0043353 | enucleate erythrocyte differentiation | 0.208885 |
| GO:0019216 | regulation of lipid metabolic process | 0.210092 |
| GO:0008285 | negative regulation of cell proliferation | 0.218457 |
| GO:0044092 | negative regulation of molecular function | 0.221191 |
| GO:0031146 | SCF-dependent proteasomal ubiquitin-dependent protein catabolic process | 0.232189 |
| GO:0045749 | negative regulation of S phase of mitotic cell cycle | 0.232189 |
| GO:0051569 | regulation of histone H3-K4 methylation | 0.232189 |
| GO:0050792 | regulation of viral reproduction | 0.251794 |
| GO:0045649 | regulation of macrophage differentiation | 0.257292 |
| GO:0045926 | negative regulation of growth | 0.274257 |
| GO:0002064 | epithelial cell development | 0.308786 |
| GO:0008361 | regulation of cell size | 0.328343 |
| GO:0043933 | macromolecular complex subunit organization | 0.33319 |
| GO:0048869 | cellular developmental process | 0.336495 |
| GO:0033044 | regulation of chromosome organization | 0.356255 |
| GO:0000079 | regulation of cyclin-dependent protein kinase activity | 0.400221 |
| GO:0051128 | regulation of cellular component organization | 0.432951 |
| GO:0006479 | protein methylation | 0.465248 |
| GO:0008213 | protein alkylation | 0.465248 |
| GO:0010948 | negative regulation of cell cycle process | 0.495482 |
| GO:0006261 | DNA-dependent DNA replication | 0.505352 |
| GO:0031060 | regulation of histone methylation | 0.537229 |
| GO:0042771 | DNA damage response, signal transduction by p53 class mediator resulting in induction of apoptosis | 0.574836 |
| GO:0043086 | negative regulation of catalytic activity | 0.589662 |
| GO:0042221 | response to chemical stimulus | 0.610839 |
| GO:0048731 | system development | 0.633564 |
| GO:0019080 | viral genome expression | 0.664594 |
| GO:0019083 | viral transcription | 0.664594 |
| GO:0048565 | digestive tract development | 0.70278 |
| GO:0044093 | positive regulation of molecular function | 0.722202 |
| GO:0007090 | regulation of S phase of mitotic cell cycle | 0.733746 |
| GO:0051568 | histone H3-K4 methylation | 0.733746 |
| GO:0030225 | macrophage differentiation | 0.777175 |
| GO:0009056 | catabolic process | 0.820035 |
| GO:0032480 | negative regulation of type I interferon production | 0.820035 |
| GO:0051090 | regulation of sequence-specific DNA binding transcription factor activity | 0.820035 |
| GO:0072332 | signal transduction by p53 class mediator resulting in induction of apoptosis | 0.820035 |
| GO:0032269 | negative regulation of cellular protein metabolic process | 0.834594 |
| GO:0009913 | epidermal cell differentiation | 0.850709 |
| GO:0043550 | regulation of lipid kinase activity | 0.863878 |
| GO:0045604 | regulation of epidermal cell differentiation | 0.863878 |
| GO:0065003 | macromolecular complex assembly | 0.881785 |
| GO:0008543 | fibroblast growth factor receptor signaling pathway | 0.907942 |
| GO:0048469 | cell maturation | 0.907942 |

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| GO:0006513 | protein monoubiquitination | 0.908039 |
| GO:0032535 | regulation of cellular component size | 0.936058 |
| GO:0043065 | positive regulation of apoptosis | 0.95315 |

Cellular Component

| GO id | GO name | adjusted-P |
|------------|--|------------|
| GO:0005654 | nucleoplasm | 7.09E-33 |
| GO:0031981 | nuclear lumen | 9.10E-32 |
| GO:0070013 | intracellular organelle lumen | 8.34E-29 |
| GO:0044428 | nuclear part | 1.03E-28 |
| GO:0043233 | organelle lumen | 1.33E-28 |
| GO:0031974 | membrane-enclosed lumen | 2.35E-28 |
| GO:0005634 | nucleus | 1.65E-23 |
| GO:0044446 | intracellular organelle part | 1.92E-18 |
| GO:0044422 | organelle part | 3.73E-18 |
| GO:0043231 | intracellular membrane-bounded organelle | 6.22E-15 |
| GO:0043227 | membrane-bounded organelle | 7.13E-15 |
| GO:0043229 | intracellular organelle | 2.26E-12 |
| GO:0043226 | organelle | 2.56E-12 |
| GO:0044451 | nucleoplasm part | 3.85E-11 |
| GO:0044424 | intracellular part | 3.86E-11 |
| GO:0005622 | intracellular | 3.49E-09 |
| GO:0043234 | protein complex | 4.14E-09 |
| GO:0005694 | chromosome | 1.15E-08 |
| GO:0044427 | chromosomal part | 2.61E-08 |
| GO:0005667 | transcription factor complex | 1.36E-07 |
| GO:0032991 | macromolecular complex | 1.67E-07 |
| GO:0000785 | chromatin | 1.26E-06 |
| GO:0005829 | cytosol | 6.95E-05 |
| GO:0000228 | nuclear chromosome | 4.95E-04 |
| GO:0044464 | cell part | 5.46E-04 |
| GO:0005623 | cell | 5.46E-04 |
| GO:0016585 | chromatin remodeling complex | 9.90E-04 |
| GO:0044454 | nuclear chromosome part | 0.004449 |
| GO:0005575 | cellular_component | 0.00678 |
| GO:0019005 | SCF ubiquitin ligase complex | 0.007329 |
| GO:0031519 | PcG protein complex | 0.017542 |
| GO:0043228 | non-membrane-bounded organelle | 0.050633 |
| GO:0043232 | intracellular non-membrane-bounded organelle | 0.050633 |
| GO:0035097 | histone methyltransferase complex | 0.067185 |
| GO:0034708 | methyltransferase complex | 0.079059 |
| GO:0016580 | Sin3 complex | 0.092563 |
| GO:0035098 | ESC/E(Z) complex | 0.092563 |
| GO:0070822 | Sin3-type complex | 0.092563 |

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| GO:0000151 | ubiquitin ligase complex | 0.099124 |
| GO:0000790 | nuclear chromatin | 0.159588 |
| GO:0017053 | transcriptional repressor complex | 0.164011 |
| GO:0016514 | SWI/SNF complex | 0.257292 |
| GO:0031461 | cullin-RING ubiquitin ligase complex | 0.418268 |
| GO:0000307 | cyclin-dependent protein kinase holoenzyme complex | 0.432984 |
| GO:0016581 | NuRD complex | 0.432984 |
| GO:0045120 | pronucleus | 0.466346 |
| GO:0015630 | microtubule cytoskeleton | 0.629481 |
| GO:0070603 | SWI/SNF-type complex | 0.908039 |

Molecular Function

| GO id | GO name | adjusted-P |
|------------|---|------------|
| GO:0005515 | protein binding | 4.08E-14 |
| GO:0008134 | transcription factor binding | 1.57E-09 |
| GO:0003712 | transcription cofactor activity | 2.81E-09 |
| GO:0000989 | transcription factor binding transcription factor activity | 3.63E-09 |
| GO:0000988 | protein binding transcription factor activity | 5.05E-09 |
| GO:0003713 | transcription coactivator activity | 1.42E-06 |
| GO:0003677 | DNA binding | 6.80E-06 |
| GO:0044212 | transcription regulatory region DNA binding | 3.55E-05 |
| GO:0019899 | enzyme binding | 4.23E-05 |
| GO:0000975 | regulatory region DNA binding | 6.34E-05 |
| GO:0001067 | regulatory region nucleic acid binding | 6.34E-05 |
| GO:0050681 | androgen receptor binding | 1.73E-04 |
| GO:0035257 | nuclear hormone receptor binding | 0.001284 |
| GO:0005488 | binding | 0.001739 |
| GO:0035258 | steroid hormone receptor binding | 0.001739 |
| GO:0051427 | hormone receptor binding | 0.002982 |
| GO:0003700 | sequence-specific DNA binding transcription factor activity | 0.003979 |
| GO:0001071 | nucleic acid binding transcription factor activity | 0.004069 |
| GO:0003676 | nucleic acid binding | 0.010705 |
| GO:0002039 | p53 binding | 0.034283 |
| GO:0019900 | kinase binding | 0.057261 |
| GO:0001047 | core promoter binding | 0.106992 |
| GO:0042826 | histone deacetylase binding | 0.114673 |
| GO:0070577 | histone acetyl-lysine binding | 0.144808 |
| GO:0001085 | RNA polymerase II transcription factor binding | 0.213874 |
| GO:0003714 | transcription corepressor activity | 0.267271 |
| GO:0008094 | DNA-dependent ATPase activity | 0.286428 |
| GO:0019901 | protein kinase binding | 0.300249 |
| GO:0001104 | RNA polymerase II transcription cofactor activity | 0.34829 |
| GO:0042393 | histone binding | 0.356255 |
| GO:0017025 | TBP-class protein binding | 0.401331 |

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| GO:0001106 | RNA polymerase II transcription corepressor activity | 0.432984 |
| GO:0001103 | RNA polymerase II repressing transcription factor binding | 0.501198 |
| GO:0001076 | RNA polymerase II transcription factor binding transcription factor activity | 0.605345 |