Supplementary Material

Genome-scale CRISPR-Cas9 knockout screening in human cells

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SUPPLEMENTARY DISCUSSIONS

GeCKO screening is carried out in three steps

Step 1 – Library Design. Constitutive exons near the 5` end of transcripts are identified using Illumina Human BodyMap 2.0 and NCBI CCDS datasets. sgRNAs were ranked by an off-target score using a metric that includes the number of off-targets in the genome and the type of mutations (distance from protospacer-adjacent motif and clustering of mismatches) and those with lowest off-target scores were selected. This resulted in a library in which most genes have an average of 3 or 4 sgRNAs.

Step 2 – Viral vector generation. The sgRNA library was synthesized using array synthesis and cloned as a pool into the lentiCRISPR transfer plasmid for virus production. Viral vectors were produced in HEK293T cells and concentrated to increase viral titer. Cells of interest were infected at a low MOI (0.3) to ensure that most cells receive only 1 viral construct with high probability.

Step 3 – Readout. 24 hours after transduction, cells were selected with puromycin so that only cells transduced with a lentiCRISPR construct are preserved. At this point the cells can be used to carry out either positive or negative selection screens.

Screening timeline considerations

After infection, cells are selected with puromycin. For most cell types, 0.5-2 ug/ml puromycin works well, although the minimum dose that kills all cells without any viral transduction should be determined in advance and the minimum concentration should be used for selection. Usually, only 2-3 days of puromycin selection is needed to select for cells with viral integration and expression but a longer period of selection has the added benefit of allowing for enough time for genome modification by Cas9.

As shown in the deep sequencing of the individual target (array) validations from the PLX resistance screen gene hits, genome modification increases over time. For most targets, genome modification was nearly complete after only 7 days. Some lentiCRISPRs had lower modification that increased by 14 days post-transduction (for example, NF1_sg4 in fig. S14, NF2_sg5 in fig. S15). As expected, for some sgRNAs, off-target modification also increases with time, albeit by a smaller amount (for example, NF2_sg4 in Fig. S14, MED12_sg2 in Fig. S15). In general, it is advisable to keep puromycin selection (and Cas9 expression since they are co-expressed) for at least 7 days post-transduction and possibly longer depending on the needs of the particular experiment.

Identification of gene candidates

Before any experiment, it is important to determine the distribution of sgRNAs before any selection pressure has been applied. This baseline sgRNA distribution will be used to infer either depletion or enrichment of specific sgRNA species.

For both positive and negative selection screens, hits are identified by comparing the distribution of sgRNAs after selection with the baseline sgRNA distribution. Candidate genes are identified by searching for sgRNAs whose frequency has either significantly reduced or increased after selection for negative and positive screens respectively.

Using multiple sgRNAs to target the same gene, and transduction replicates are the main experimental features that enable discrimination between true and false positive hits. The reason is that each screen will have some background rate, meaning that with some probability an sgRNA can be enriched (or depleted) despite having no effect on the studied phenotype. The required number of unique sgRNAs for the same genes should be determined by the background rate of the screen and the overall efficacy of sgRNAs. As increasing sgRNA numbers per gene comes with a cost of increasing library complexity, additional infection replicates can compensate for it as long as there is a minimal number of sgRNAs that can effectively mediate gene targeting.

Finally, ranking of the top hits requires the conversion of sgRNA scores into gene rankings. A simple method is to rank gene hits according to the mean or median of all sgRNAs for each respective gene. We recommend combining this simple method with other analysis such as RIGER (*1*) and RSA (*2*).

GeCKO versus shRNA screening

GeCKO screening operates through a fundamentally different mechanism than shRNA based screening. Whereas shRNAs reduce protein expression by targeting the mRNA, GeCKO achieves protein knockdown via frameshift mutations introduced into the genomic coding region. GeCKO-mediated frameshift mutations are achieved through targeted DNA double strand breaks (DSB) and subsequent mutagenic repair via the non-homologous end joining (NHEJ) pathway, which produces indels at the site of DSB. The indel being introduced into the DSB is random (fig. S16), with some indels leading to frameshift mutations that cause premature termination of the transgene. Other indels with lengths that are multiples of three will not result in the frameshift of the candidate genes. In this scenario, the gene product might still be functional. In contrast, shRNA knockdown can generate a spectrum of expression levels of the target genes. Therefore GeCKO screening can provide potential advantages over shRNA, where the population of cells that has been homozygously knocked out can provide more screening sensitivity especially when probing gene products that can function normally even at significantly reduced concentrations.

Vemurafenib (PLX) resistance mechanisms

The protein kinase BRAF, a key regulator of the MAPK signaling cascade, is mutated in more than half of malignant melanomas and in several other types of cancer, such as thyroid, colorectal, lung, and hairy cell leukemia (*3*). The V600E mutant form of BRAF is a common gain of function mutation that allows BRAF to remain in a constitutively active state and phosphorylate MEK without forming a phosphorylated BRAF dimer (*4*). Vemurafenib (PLX) is a FDA-approved, ATP-competitive RAF inhibitor that displays higher binding affinity for V600E mutant BRAF over other RAF isoforms, including wild-type BRAF (*5*). Over 50% of melanoma patients with mutated BRAF treated with PLX display tumor reduction, but the effect is short-lived and resistance develops in a majority of cases (*6-8*). By applying the GeCKO library to A375 cells (which are homozygous for the BRAF V600E mutation), we identified several genes whose loss resulted in resistance to PLX.

In the PLX screen, we identified and validated NF2, NF1, MED12, CUL3, TADA1, and TADA2B as genes whose loss results in PLX resistance. Loss of NF1 and MED12 were previously identified resistance mechanisms from two separate, large-scale RNAi screens (*9, 10*). MED12, a member of the Mediator transcription complex, is a negative regulator of TGF-βR and its loss results in activation of TGF-βR signaling and MEK/ERK (*10*). NF1 is a negative regulator of NRAS activity and its loss phenocopies activating NRAS mutations (*9, 11*), an established PLX resistance mechanism (*12, 13*).

Although they have similar names, NF1 and NF2 are tumor suppressors that function via distinct pathways. NF2 (or Merlin, Moesin-Ezrin-Radixin-Like Protein) is a tumor suppressor gene that encodes a cytoskeletal protein (*14*). Loss of NF2 leads to constitutive mTOR activation and cell proliferation by a MEK/ERK-independent mechanism (*15*) and involves the Hippo signaling pathway (*16, 17*). Mutation and copy number variation of the E3 ligase CUL3 has been described in lung squamous cell carcinomas and renal cell carcinomas (*18, 19*). Quantitative proteomics in T24T bladder cancer cells found that silencing of CUL3 restored the expression of cytoskeleton proteins that are underexpressed in T24T, such as moesin and erzin (*20*). This suggests a possible interaction between CUL3 and NF2/merlin, a similar cytoskeletal protein to those ubiquitinated by CUL3.

TADA1 and TADA2B are chromatin-modifying enzymes involved in transcription and are members of the multiprotein STAGA (SPT3-TAF9-GCN5-acetylase) complex. The STAGA complex recruits Mediator complex proteins (such as MED12) to the oncoprotein c-Myc to activate proliferation (*21*). Although we did not attempt to validate it, CCDC101 had a high RIGER rank in both infection replicates (see table S6) and is also a subunit of the STAGA complex and thus may lead to PLX resistance through a similar mechanism as TADA1 and TADA2B.

Since many of the gene hits from the PLX screen interact with each other and are involved in established cell proliferation pathways, therapeutics targeted to these pathways could be combined with BRAF inhibition to achieve better clinical outcomes in melanoma and other cancers.

Other applications of GeCKO screening

In addition to facilitating loss-of-function gene screening, GeCKO and similar Cas9-sgRNA libraries can be customized to carry out a variety of genome-scale perturbations to study the effect of non-coding elements, transcriptional changes, and epigenetic modulations.

In this library, we target the constitutive exons near the 5` end of genes for loss-of-function but sgRNAs can also be targeted to promoters, enhancers, intronic, and intergenic regions. Screens targeting non-coding regions or a mix of coding and non-coding regions can elucidate how these different elements contribute to gene expression and biological function.

As we and other groups have recently shown (*22-26*), Cas9 with mutated catalytic residues can be fused to a transcriptional activation domain such as VP16 or repressor domain such as SID4X or KRAB to create a Cas9 transcriptional modulator without any nuclease activity. By replacing the Cas9 in the lentiCRISPR plasmid with a null-nuclease version (eg. with D10A and H840A mutations) (*27, 28*), libraries of sgRNAs for activation can be used to investigate how activation of different transcripts or different splice variants contribute to a screen phenotype. A null-nuclease Cas9 could also be fused with different effector domains capable of modifying the epigenetic state at a particular locus. Previous work from our group and others has demonstrated transcriptional changes using zinc-finger proteins and transcriptional activator like effectors (TALEs) fused to histone (de)acetylases, histone (de)methylases, DNA (de)methylases and other epigenetic modifiers (*23, 29, 30*). The easy programmability of Cas9 DNA binding using sgRNAs that can be array synthesized *en masse* opens up many new possibilities for genome-scale screens.

SUPPLEMENTARY MATERIALS AND METHODS

GeCKO library design

A genome-scale sgRNA library was constructed as follows: First, early constitutive exons were identified for all coding genes. Then, sgRNAs to target these early constitutive exons were selected by choosing sgRNAs that were predicted to have minimal off-target activity.

To identify constitutive exons, RNA sequencing data from the Illumina Human Body Map 2.0 (GEO accession number: GSE30611) was mapped to the reference human genome (hg19) using TopHat v1.0.14 (*31*) and transcripts were reconstructed with Cufflinks v1.0.2 (*32*), as previously described (*33*). Exons expressed across all tissues in the Illumina dataset were chosen as constitutive exons for sgRNA targeting. In addition, for each gene, the first and last exons were excluded along with any exon that contained an alternative splicing site.

For the constitutive exons, genomic sequences were retrieved from the NCBI Consensus CoDing Sequence database (http://www.ncbi.nlm.nih.gov/CCDS/). For each CCDS entry, the two earliest constitutive exons were chosen as candidate exons for library design. For genes without RNA sequencing data or where no exons qualified as constitutive, exons 2 and 3 were included as candidate exons for library design.

Next, for each candidate exon, all possible *S. pyogenes* Cas9 sgRNA sequences of the form $(N)_{20}NGG$ were listed as candidate targets. Each 20mer candidate sgRNA was mapped to a precompiled index containing all 20mer sequences in the human genome followed by either NGG or NAG. This mapping was done using Bowtie short read aligner (*34*), allowing up to 3 base mismatches.

The following heuristic was used to rank sgRNAs for each exon based on recent work that characterized the sequence specificity of Cas9 nuclease (*25, 35, 36*). First, any sgRNAs with other targets in the genome that match exactly or differ by only 1 base are discarded. For the remaining sgRNAs, we calculate the following off target score:

$$OS = \sum_{off\ targets} (sum\ mm\ location)\left({}^{D(mm)}/_{D(max)}\right)$$

sum mm location = sum of the mismatch locations from 3’ to 5’. The PAM (NGG) proximal base is 1 and the PAM distal base is 20.
D(mm) = distance in bp between mismatch locations.
D(max) = maximal possible distance between 2 or 3 mismatches.

When mismatches are clustered more closely together, the cutting efficiency of Cas9 is significantly lower (*35*). Therefore, in the *OS*, the location of mismatches is weighted by their distances from each other. For each gene, the best (lowest *OS*) sgRNAs were chosen with the constraint that no sgRNAs have a *OS*>400. This resulted in a library of 64,751 unique sgRNAs targeting 18,080 coding genes with an average of 3-4 sgRNAs per gene. For all sgRNAs, an extra 5’ G was added to improve U6 transcription.

Array oligo synthesis and pooled library cloning

DNA oligonucleotide library synthesis was performed on a programmable microarray using a B3 Synthesizer (CustomArray) and SAFC Proligo reagents (Sigma), as recommended by the manufacturer. The synthesis products were cleaved from the microarray and deprotected by overnight incubation in 28-30% ammonium hydroxide at 65 °C, dried, resuspended in TE buffer and then purified using a QIAquick spin column (Qiagen). Full-length oligonucleotides (74 nt) were amplified by PCR using Phusion HS Flex (NEB) and size-selected using a 2% agarose E-Gel EX (Life Technologies, Qiagen).

ArrayF	`TAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTGTGGAAAGGACGAAACACCG`
ArrayR	`ACTTTTTCAAGTTGATAACGGACTAGCCTTATTTTAACTTGCTATTTCTAGCTCTAAAAC`

The lentiCRISPR vector was digested with BsmBI (Fermentas) and treated with alkaline phosphatase (Fermentas) at 37°C for 2 hours and gel-purified on a 1 % E-Gel EX (Life Technologies, Qiagen). A 20 ul Gibson ligation reaction (NEB) was performed using 10 ng of the gel-purified inserts and 25 ng of the vector. From the ligation, 0.5 ul of the reaction was transformed into 25 ul of electrocompetent cells (Lucigen) according to the manufacturer's protocol using a GenePulser (BioRad). To ensure no loss of representation, 36 parallel transformations were performed using the same ligation reaction and plated onto 245 mm x 245 mm plates (Corning) with carbenicillin selection (50 ug/ml), which yielded 166 X library coverage. Colonies were scraped off plates and combined before plasmid DNA extraction using Endotoxin-Free Plasmid Maxiprep (Qiagen).

Lentivirus production and purification

To produce lentivirus, twelve T-225 flasks of HEK293T cells (Broad RNAi Platform) were seeded at ~40 % confluence the day before transfection in D10 media (DMEM supplemented with 10 % fetal bovine serum). One hour prior to transfection, media was removed and 13 mL of pre-warmed reduced serum OptiMEM media (Life Technologies) was added to each flask. Transfection was performed using Lipofectamine 2000 and Plus reagent (Life Technologies). For each flask, 200 ul of Plus reagent was diluted in 4 ml OptiMEM (Life Technologies) with 20 ug of lentiCRISPR plasmid library, 10 ug of pVSVg, and 15 ug of psPAX2 (Addgene). 100 ul of Lipofectamine 2000 was diluted in 4 ml OptiMEM and, after 5 min, it was added to the mixture of DNA and Plus reagent. The complete mixture was incubated for 20 min before being added to cells. After 6 h, the media was changed to 30 ml D10 supplemented with 1 % BSA (Sigma).

After 60 h, the media was removed and centrifuged at 3,000 rpm at 4 °C for 10 min to pellet cell debris. The supernatant was filtered through a 0.45 um low protein binding membrane (Millipore Steriflip HV/PVDF). To achieve 300 X concentration of the GeCKO pooled library, the virus was ultracentrifuged (Sorvall) at 24,000 rpm for 2 h at 4 °C and then resuspended overnight at 4 °C in D10 supplemented with 1% BSA. Aliquots were stored at –80°C.

Cell transduction using the GeCKO library

Cells were transduced with the GeCKO library via spinfection. To find optimal virus volumes for achieving an MOI of 0.3–0.5, each new cell type and new virus lots were tested by spinfecting 3x10^6 cells with several different volumes of virus. Briefly, 3x10^6 cells per well were plated into a 12 well plate in the appropriate standard media for the cell type (see below) supplemented with 8 ug/ml polybrene (Sigma). For A375 cells (ATCC), standard media was R10: RPMI 1640 supplemented with 10 % FBS. For HUES62 (Harvard Stem Cell Institute iPS Core Facility), standard media consists of mTeSR1 (STEMCELL Technologies) supplemented with 1X Normocin (InvivoGen). Each well received a different titrated virus amount (usually between 5 and 50 ul) along with a no-transduction control. The 12-well plate was centrifuged at 2,000 rpm for 2 h at 37°C. After the spin, media was aspirated and fresh media (without polybrene) was added.

Cells were incubated overnight and then enzymatically detached using trypsin (Corning) for A375 and Accutase (STEMCELL) for HUES62. Cells were counted and each well was split into duplicate wells. One replicate received 0.5 ug/mL puromycin (Sigma) for HUES62 cells or 1 ug/ml puromycin for A375 cells. After 3 days (or as soon as no surviving cells remained in the no-transduction control under puromycin selection), cells were counted to calculate a percent transduction. Percent transduction is calculated as cell count from the replicate with puromycin divided by cell count from the replicate without puromycin multiplied by 100. The virus volume yielding a MOI closest to 0.4 was chosen for large-scale screening.

Large-scale spinfection of 5x10^7 to 1x10^8 A375 or HUES62 cells was carried out in the same way as described above using 12-well plates with 3x10^6 cells per well. Wells were pooled together into larger flasks on the day after spinfection.

HUES62 depletion screen

6x10^7 HUES62 human embryonic stem (hES) cells were transduced as described above. 30uL of the concentrated GECKO library was applied to each well containing 3x10^6 cells, resulting in an transduction efficiency of 30 % (approximately 270 cells per lentiCRISPR construct). Puromycin (0.5 ug/mL) was added to the cells 24 hours post transduction and maintained for 7 days. On day 7, cells were split into replicate flasks with a minimum of $2x10^7$ cells per replicate and cultured for an additional 14 days before genomic DNA extraction and analysis. During the screen, hES cells were fed daily with mTeSR1.

A375 PLX-4032 resistance screen

$8x10^7$ A375 cells were transduced as described above with $2x10^6$ cells plated per transduction well. 10 uL of the concentrated GECKO library was applied to each well containing $2x10^6$ cells, attaining a transduction efficiency of 30 % (approximately 370 cells per lentiCRISPR construct). Puromycin (1 ug/mL) was added to the cells 24 hours post transduction and maintained for 7 days. On day 7, cells were split into drug conditions in duplicate with a minimum of $2.6x10^7$ cells per replicate and an additional $3x10^7$ cells were frozen down for genomic DNA analysis. Two replicates were cultured in R10 supplemented with 2uM PLX4032 (Selleckchem) and two replicates were cultured in R10 supplemented with an equal volume DMSO (Sigma Aldrich). Replicates were either passaged or fresh media was added every 2-3 days. Cell pellets with a minimum of $3x10^7$ cells were taken at 7 days after drug addition and 14 days after drug addition at which point the screen was terminated.

Genomic DNA sequencing

Frozen cell pellets were thawed and genomic DNA was extracted with a Blood & Cell Culture Midi kit (Qiagen). PCR was performed in two steps: For the first PCR, the amount of input genomic DNA (gDNA) for each sample was calculated in order to achieve 300X coverage over the GECKO library, which resulted in 130 ug DNA per sample (assuming 6.6 ug of gDNA for 10^6 cells). For each sample, we performed 13 separate 100 ul reactions with 10 ug genomic DNA in each reaction using Herculase II Fusion DNA Polymerase (Agilent) and then combined the resulting amplicons. Primers sequences to amplify lentiCRISPR sgRNAs for the first PCR are:

F1 `AATGGACTATCATATGCTTACCGTAACTTGAAAGTATTTCG`

R1 `CTTTAGTTTGTATGTCTGTTGCTATTATGTCTACTATTCTTTCC`

A second PCR was performed to attach Illumina adaptors and to barcode samples. The second PCR was done in a 100 ul reaction volume using 5ul of the product from the first PCR. Primers for the second PCR include both a variable length sequence to increase library complexity and an 8bp barcode for multiplexing of different biological samples:

F2 `AATGATACGGCGACCACCGAGATCTACACTCTTTCCCTACACGACGCTCTTCCGATCT(1-9bp variable length sequence)(8bp barcode)tcttgtggaaaggacgaaacaccg`
R2 `CAAGCAGAAGACGGCATACGAGATGTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTtctactattctttcccctgcactgt`

Resulting amplicons from the second PCR were gel extracted, quantified, mixed and sequenced using a HiSeq 2500 (Illumina). Amplification was carried out with 18 cycles for the first PCR and 24 cycles for the second PCR.

Data processing and initial analysis

Raw FASTQ files were demultiplexed using the FASTX-Toolkit (http://hannonlab.cshl.edu/fastx_toolkit/) and processed to contain only the unique sgRNA sequence. To align the processed reads to the library, the designed sgRNA sequences from the library were assembled into a Burrows-Wheeler index using the Bowtie `build-index` function. Reads were then aligned to the index using the Bowtie aligner. After alignment, the number of uniquely aligned reads for each library sequence was calculated.

The numbers of reads for each unique sgRNA for a given sample were normalized as follows:

$$normalized\ reads\ per\ sgRNA = \frac{reads\ per\ sgRNA}{total\ reads\ for\ all\ sgRNAs\ in\ sample} \times 10^6 + 1$$

Array lentiCRISPR array screen

Individual lentiCRISPRs from the GECKO pool were produced as above except that viral supernatants were not concentrated by ultracentrifugation. For each lentiCRISPR, 5x10^5 A375 cells were infected via spinfection at 2,000 rpm for 2 h at 37°C in R10 supplemented with 8ug/ml polybrene. After 14 days of puromycin selection, infections were plated into separate dishes for Western blotting and the cell viability assay.

Western blotting

A375 cells were lysed in Cell Lysis Buffer (Cell Signaling 9803) with protease inhibitors (Sigma P8340). Lysates were homogenized using a Bioruptor sonicator (Diagenode) for 5 minutes (30s on-30s off cycle, high power) and then centrifuged at 15,000 rpm for 20 min at 4 °C. Supernatants were quantified using the BCA assay (Thermo/Pierce). 20ug of protein was denatured at 70C for 10 minutes before gel electrophoresis on a 4-12 % Bis-Tris gel (Life Technologies). Proteins were transferred to nitrocellulose membranes at 60V overnight at 4 °C. Antibodies used: Anti-NF2 (1:1000, Abcam ab109244), Anti-NF1 (1:1000, Abcam ab17963), Anti-MED12 (1:1000, Cell Signaling 4529S), Anti-CUL3 (1:1000, Cell Signaling 2759S), Anti-TADA2B (1:1000, Sigma HPA035770), Anti-GAPDH (1:5000, Cell Signaling 3683S). Membranes were developed by SuperSignal West Femto ECL (Thermo/Pierce) and imaged using BioRad ChemiDoc MP imaging system.

Cell viability assay

lentiCRISPR-infected A375 cells were plated in quadruplicate into 96-well plates at a density of 5 x 10^3 cells per well. Either PLX or vehicle (DMSO) was added 1 day after plating. PLX was added at the following concentrations: 20 nM, 200 nM, 2 uM, 20 uM, and 200uM. Drug/vehicle was renewed every 2-3 days using a Janus liquid handler (PerkinElmer).

After 5 days of drug/vehicle treatment, cell viability was measured using CellTiter Glo (Promega). After allowing cells to reach room temperature, media was aspirated from the cells and CellTiter Glo (diluted 1:4 in phosphate-buffered saline) was added. Plates were placed on an orbital shaker for 2 min followed by a 10 min room temperature incubation. Luminescence was read out on an EnVision plate imager (PerkinElmer).

Flow cytometry analysis of GFP knockout or knockdown

lentiCRISPR with sgRNAs targeting EGFP were cloned using the following sequences (annotated in fig. S1):

`EGFP sgRNA 1`	`GGGCGAGGAGCTGTTCACCG`
`EGFP sgRNA 2`	`GAGCTGGACGGCGACGTAAA`
`EGFP sgRNA 3`	`GGCCACAAGTTCAGCGTGTC`
`EGFP sgRNA 4`	`GGAGCGCACCATCTTCTTCA`
`EGFP sgRNA 5`	`GAAGTTCGAGGGCGACACCC`
`EGFP sgRNA 6`	`GGTGAACCGCATCGAGCTGA`

Four shRNAs targeting EGFP in a pLKO (puromycin-selectable) vector were used (Broad RNAi Platform):

`EGFP shRNA 1`	`TRCN0000072194`
`EGFP shRNA 2`	`TRCN0000072181`
`EGFP shRNA 3`	`TRCN0000072201`
`EGFP shRNA 4`	`TRCN0000072198`

Control lentiCRISPR contained no spacer sequence and control shRNA was null hairpin TRCN0000208001.

For both lentiCRISPRs and shRNAs, virus was produced using a similar protocol as presented above but without ultracentrifuge purification. HEK293T cells with a single copy of EGFP (Broad RNAi Platform) were infected on Day 0 and then analyzed by flow cytometry on Day 5 and Day 11 post-infection. Flow cytometry was performed on a BD Accuri C6 cytometer in 96-well plates. Analysis was done in FlowJo (Treestar) by first gating for viable cells using forward and side scatter and then gating the fluorescence histogram.

Sequencing data analysis and indel detection

Off target loci in the human genome were identified for individual spacers using the CRISPR design tool (http://tools.genome-engineering.org) (*37*). On-target and off-target loci were PCR amplified using Herculase II Fusion polymerase (Agilent), normalized, and pooled in equimolar proportions. Pooled libraries were denatured, diluted to a 14pM concentration and sequenced using the MiSeq Personal Sequencer (Illumina). Sequencing data was demultiplexed using paired barcodes, aligned to reference amplicons, and analyzed for indels as described previously (*35*). Indel length analysis was performed by mapping the distance between multiple short reference sequences in individual reads.

SUPPLEMENTARY FIGURES

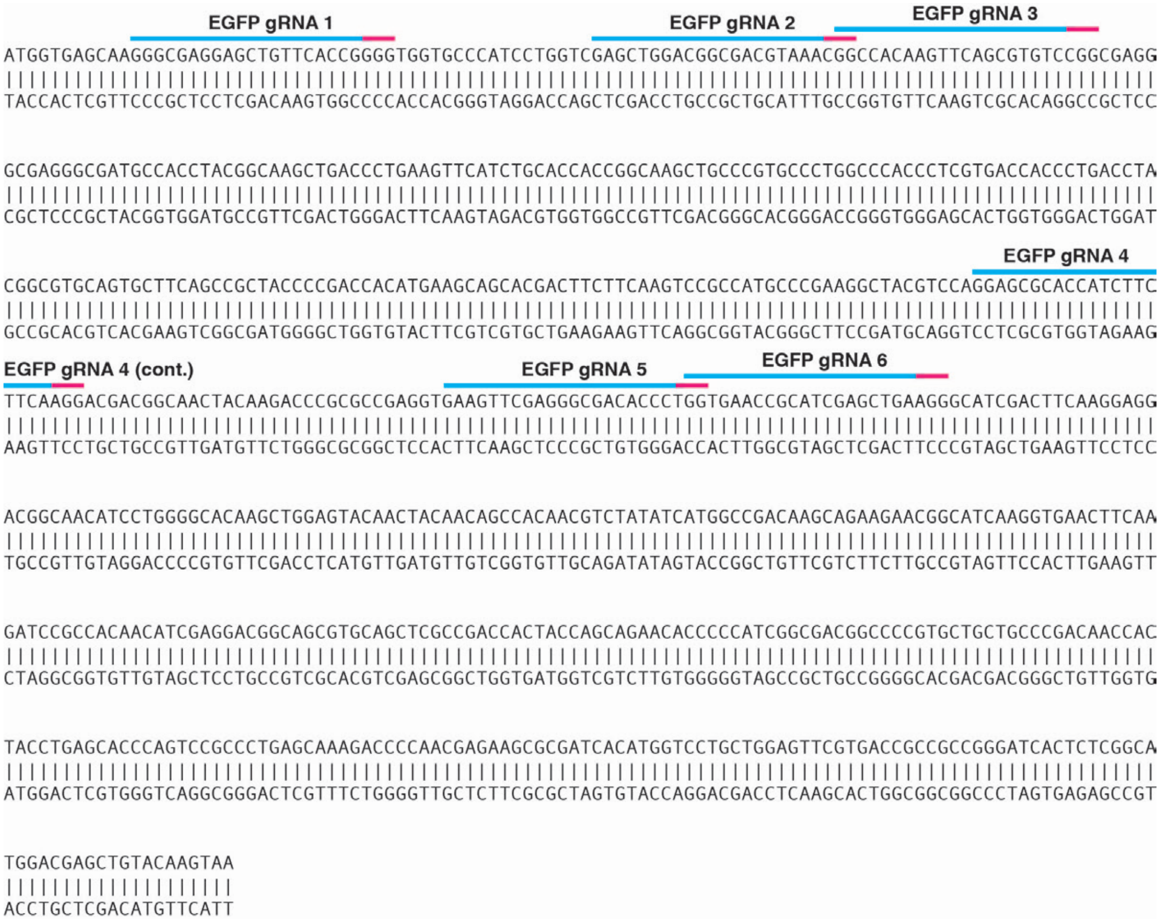

Fig. S1 | Design of sgRNAs to knock out EGFP

EGFP sequence is shown with six different sgRNAs that were designed to target the coding sequence.

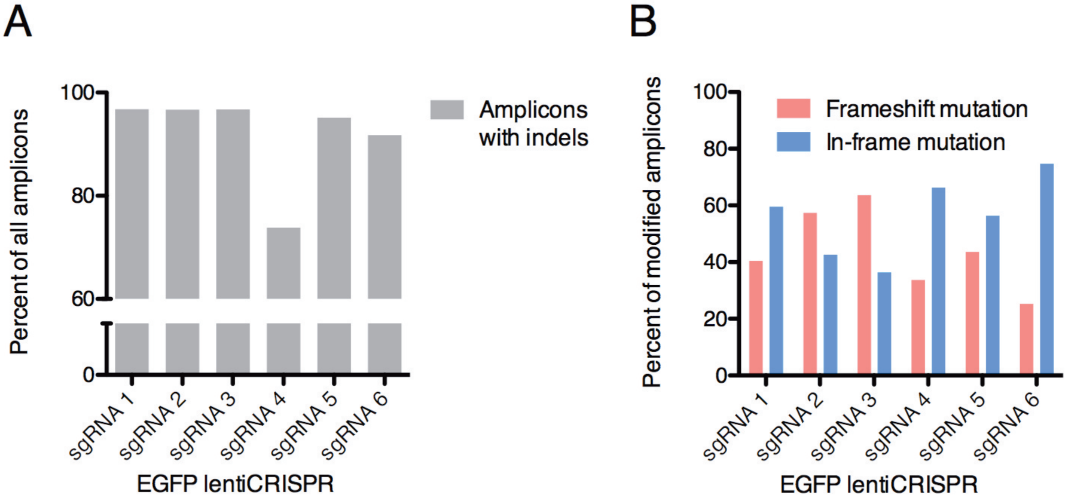

Fig. S2 | Deep sequencing for indel analysis of EGFP locus after lentiCRISPR modification

(**A**) Deep-sequencing of genomic DNA from HEK293T-EGFP cells that were infected with EGFP-targeting lentiCRISPRs shows that most amplicons have insertion or deletion (indel) mutations. Genomic DNA was extracted from cells on day 11 post-infection. For each lentiCRISPR, 1-2x10^4 reads were used for the analysis. (**B**) Distribution of types of indel mutations. lentiCRISPR transduction leads to both frameshift and in-frame indel mutations.

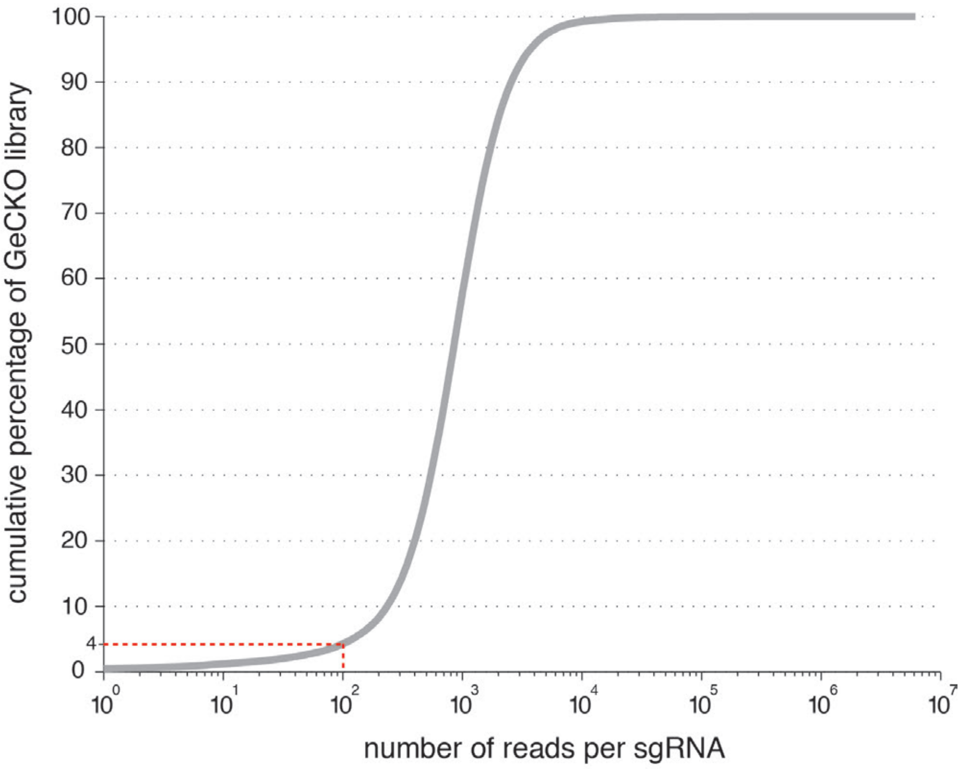

Fig. S3 | Read coverage per sgRNA in a single experiment

Cumulative distribution of the number of reads per sgRNA in a single A375 experiment. The red line indicates that less than 4% of the sgRNAs are covered by less than 100 reads.

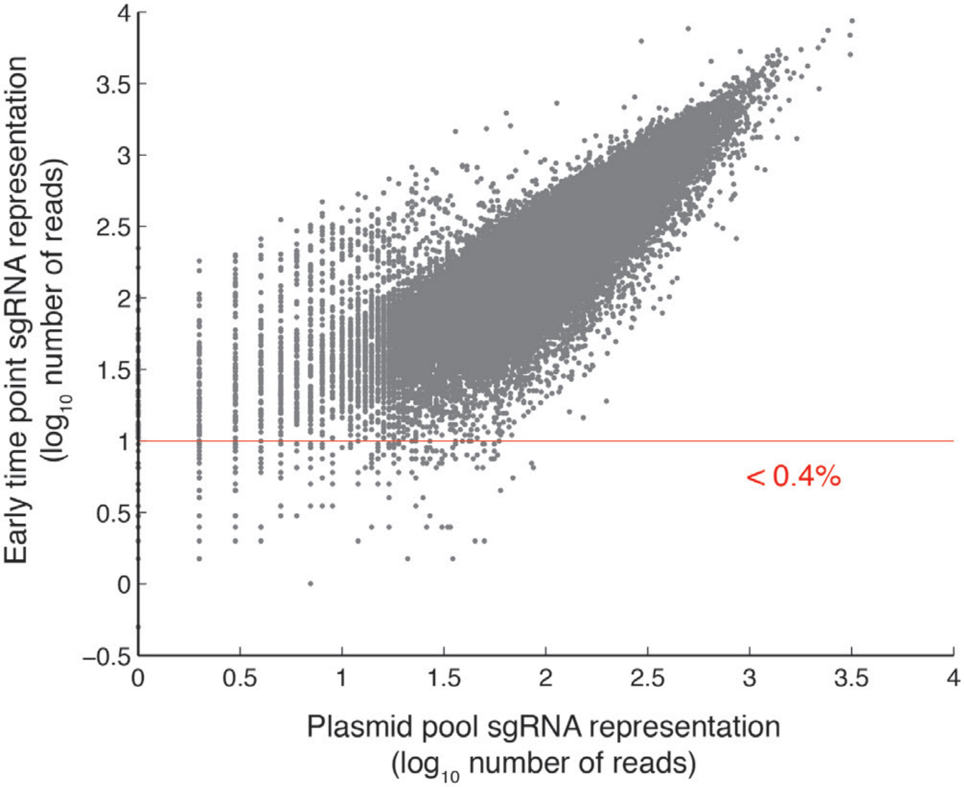

Fig. S4 | Comparison of sgRNA representation between the plasmid pool to an early time point (day 7)

Scatter plot of sgRNA representation ($\log_{10}$ number of reads) between the plasmid pool before virus production to a cell population 7 days post infection. Red line indicates that less than 0.4% of sgRNA have undetectable representation (less than 10 reads).

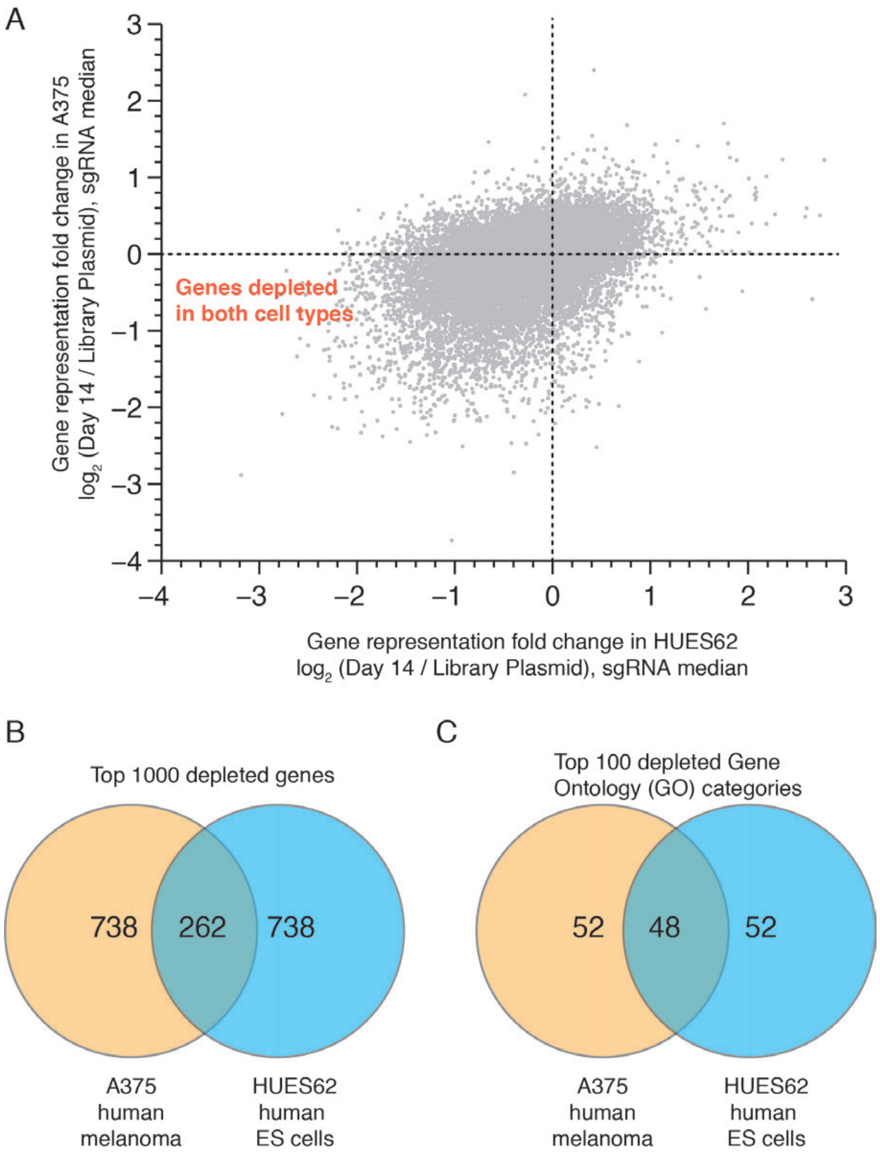

Fig. S5 | Comparison of gene and gene category depletion between A375 melanoma and HUES62 human ES cells

(**A**) Scatter plot of gene enrichment/depletion as $\log_2$ fold change of each gene between cells 14 days post-transduction and initial library plasmid in A375 melanoma cells and HUES62 hES cells. Gene enrichment/depletion was calculated using RIGER analysis of individual sgRNA depletion. Lower left quadrant contains genes depleted in both A375 and HUES62 cells. (**B**) Overlap between the top 1000 most depleted genes in each cell type. (**C**) Overlap between the top 100 most depleted Gene Ontology (GO) categories for each cell type as ranked by Gene Set Enrichment Analysis (GSEA) on the gene enrichment/depletion values.

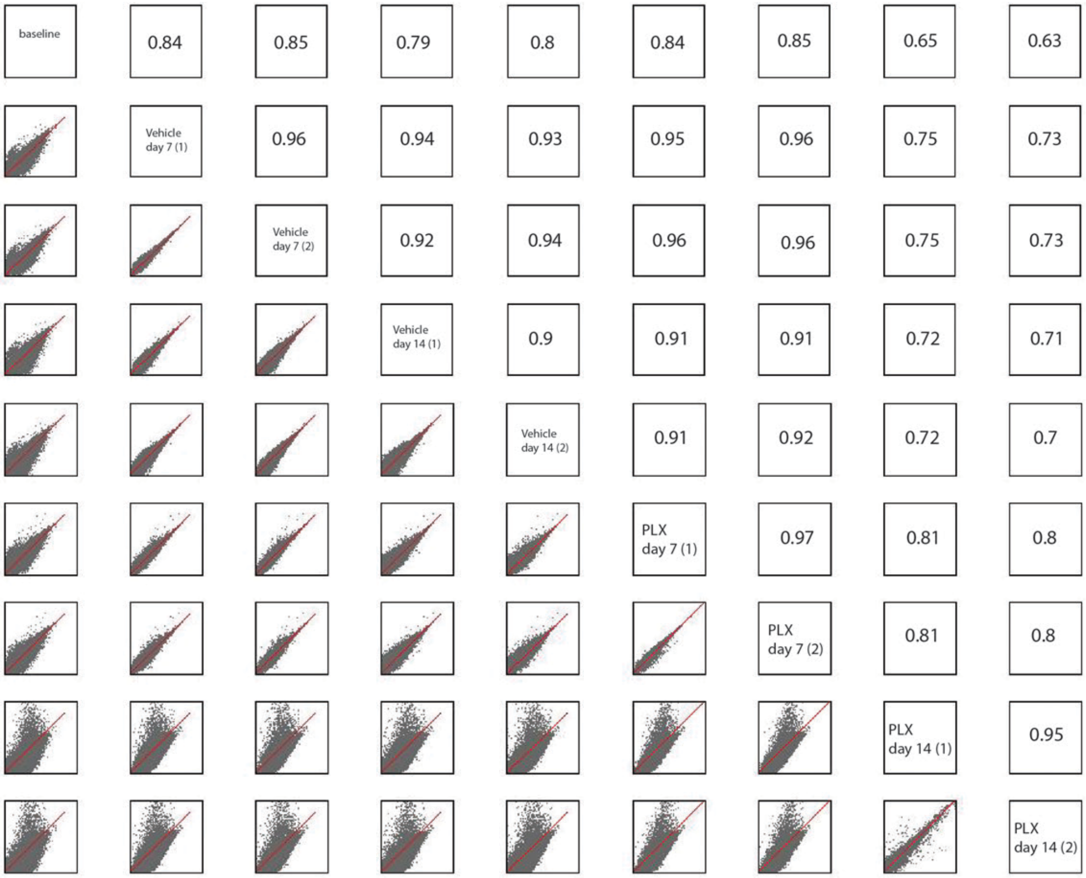

Fig. S6 | Comparison of different treatment conditions and biological replicates in the first A375 PLX screen

Each square in the lower left half of the matrix compares the normalized sgRNA read count between two biological samples. Sample labels for each axis are indicated on the diagonal. For example, the box on the second row from the bottom and third column from the right compares PLX day 7 (2) on the x-axis with PLX day 14 (1) on the y-axis. The Pearson correlation coefficient for comparison (*i,j*) can be found in box (*j,i*); for the example described in the previous sentence, the correlation coefficient is 0.81.

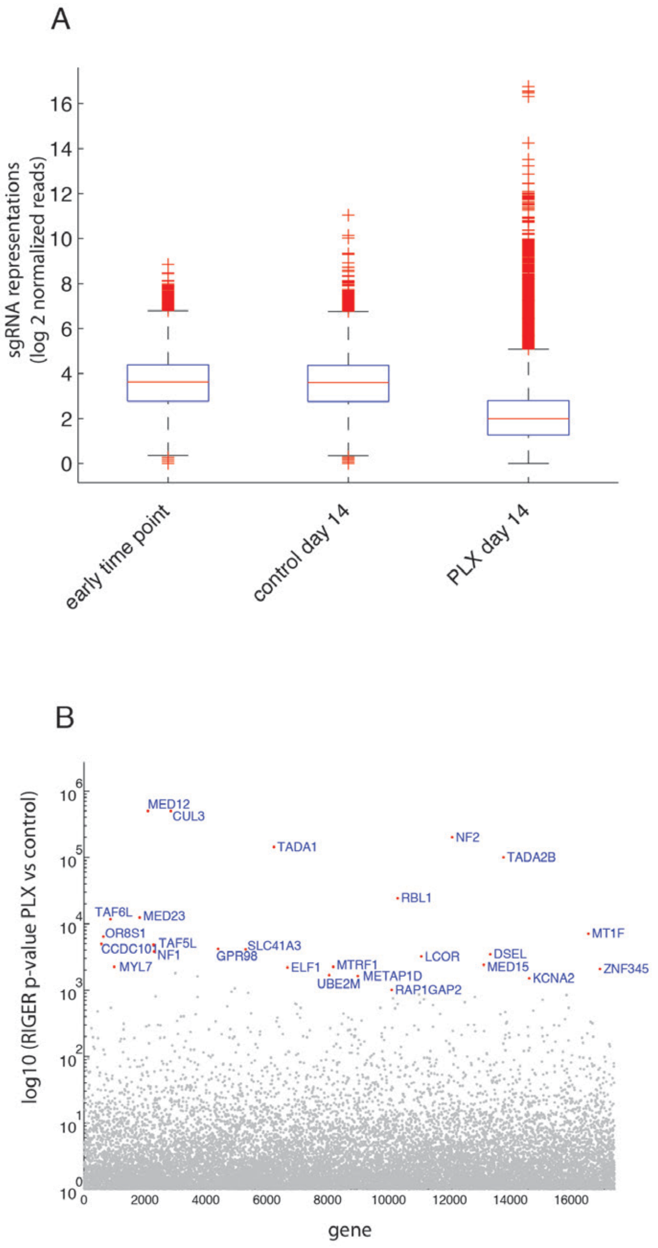

Fig. S7 | sgRNA and gene enrichment from the second A375 PLX screen

(**A**) Boxplot showing the distribution of reads from individual sgRNAs for the early timepoint, DMSO treated control, and PLX-4023 (PLX) treatment. The box extends from the first to the third quartile with the whiskers denoting 1.5 times the interquartile range. After 14 days of PLX treatment, while there is a decrease in the average number of reads per sgRNA, there is an increase in the number of reads for the most abundant sgRNAs. (**B**) Plot of the RIGER *p* value for genes enriched in PLX compared to vehicle control.

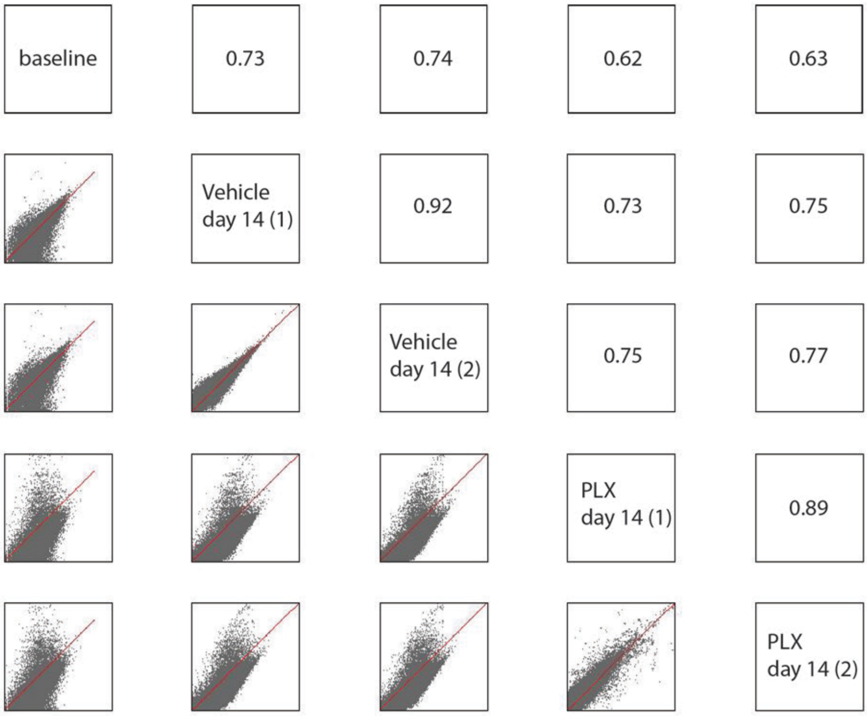

Fig. S8 | Comparison of different treatment conditions and biological replicates in the infection replicate A375 screen

Each square in the lower left half of the matrix compares the normalized sgRNA read count between two biological samples. Sample labels for each axis are indicated on the diagonal. For example, the box on the second row from the bottom and third column from the right compares Vehicle day 14 (2) on the x-axis with PLX day 14 (1) on the y-axis. The Pearson correlation coefficient for comparison (*i,j*) can be found in box (*j,i*); for the example described in the previous sentence, the correlation coefficient is 0.75.

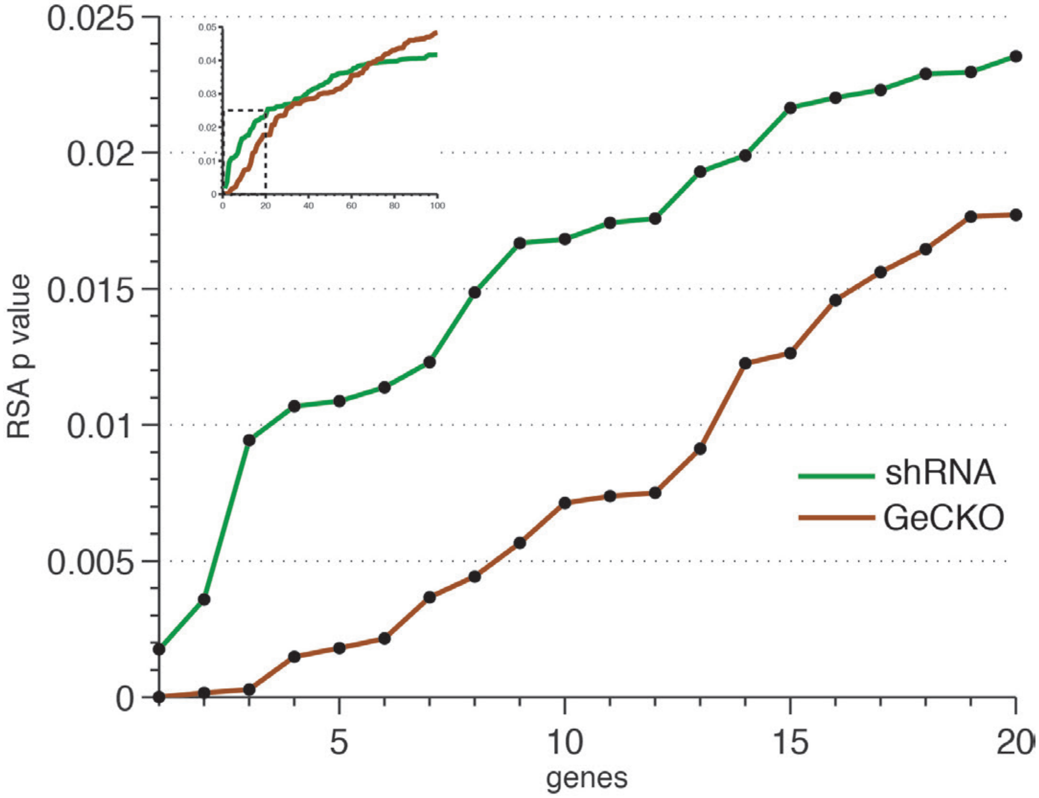

Fig. S9 | Cumulative *p* value distribution for the top hits as determined by the Redundant siRNA Activity (RSA) algorithm

Lower *p* values signify a higher consistency of distinct reagents targeting the same genes. RSA calculates the significance of reagents concentrated near the top or bottom of an enrichment list through an iterative hypergeometric test (*2*).

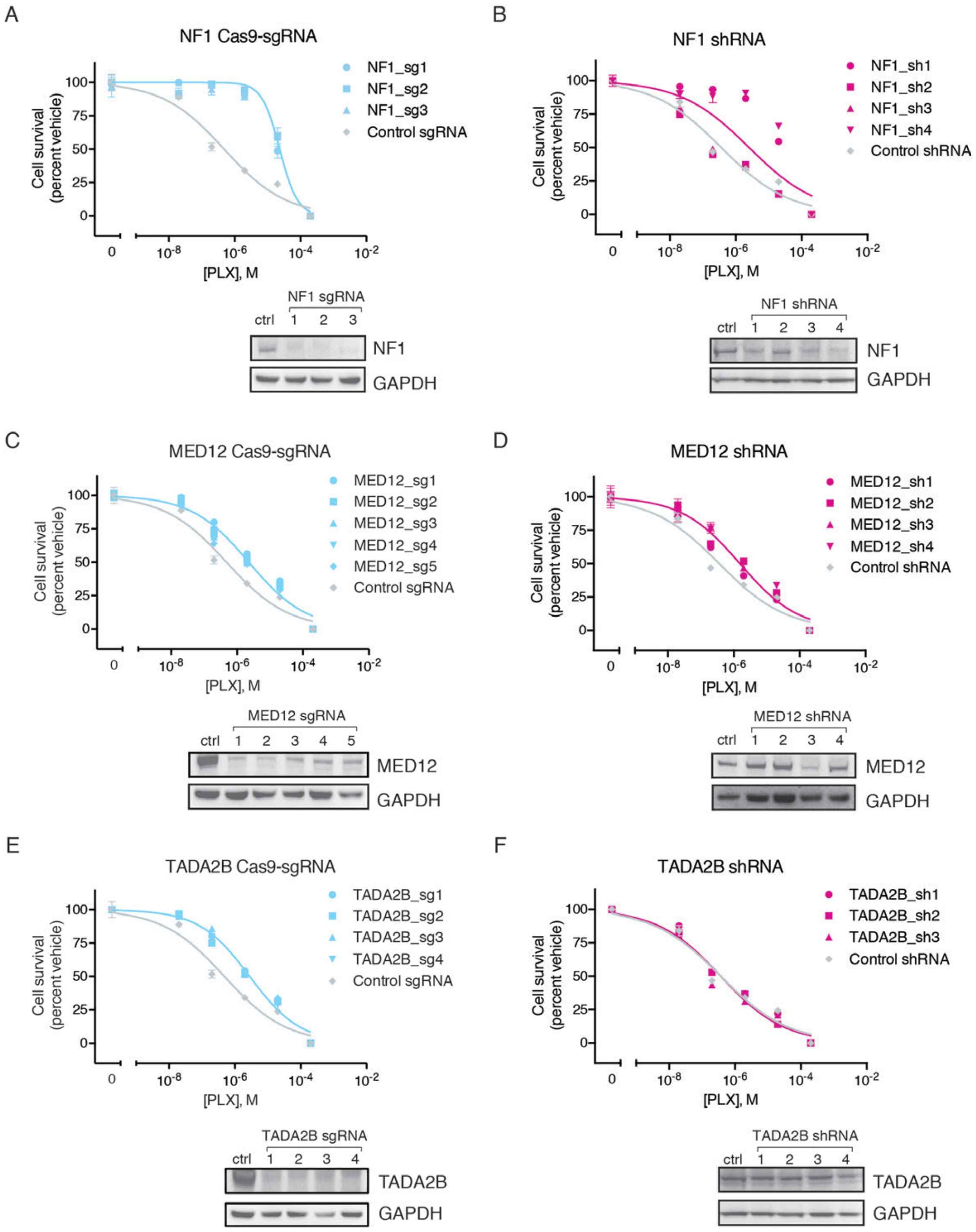

Fig. S10 | Array validation and comparison of the three highest-ranking genes using both CRISPR and shRNAs

Each panel shows cell survival data at different PLX doses as determined by CellTiter-Glo and protein quantification using western analysis. The gray line shows the mean of 2 control sgRNAs (targeting EGFP) or 2 control shRNAs (pLKO-nullT control vectors) and the colored line (blue for Cas9-sgRNAs, pink for shRNAs) shows the mean of all targeting reagents for the gene. *n* =4 replicates for dose response data. Shift in the dose response curve to the right of the control curve indicates greater resistance to PLX in the perturbed cell lines. (**A**), (**B**) Cas9-sgRNA and shRNA reagents respectively targeting *NF1*. (**C**), (**D**) Cas9-sgRNA and shRNA reagents respectively targeting *MED12*. (**E**), (**F**) Cas9-sgRNA and shRNA reagents respectively targeting *TADA2B* gene.

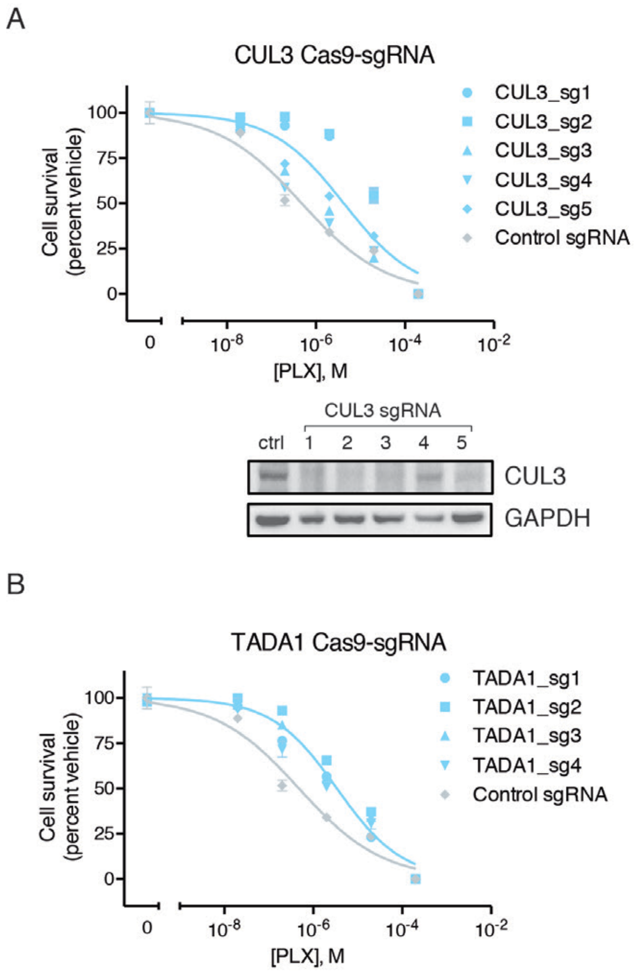

Fig. S11 | Array validation of the two additional high-ranking genes

Each panel shows cell survival data at different PLX doses as determined by CellTiter-Glo and protein quantification using western analysis. The gray line shows the mean of 2 control sgRNAs that target *EGFP* and the blue line shows the mean of Cas9-sgRNAs targeted to the gene. Shift in the dose response curve displays the reduced sensitivity to PLX in the perturbed cell lines. (**A**) Cas9-sgRNAs targeting *CUL3*. (**B**) Cas9-sgRNAs targeting *TADA1*. Western analysis was not performed for *TADA1* since neither of the two antibodies attempted yielded a band of the correct molecular weight.

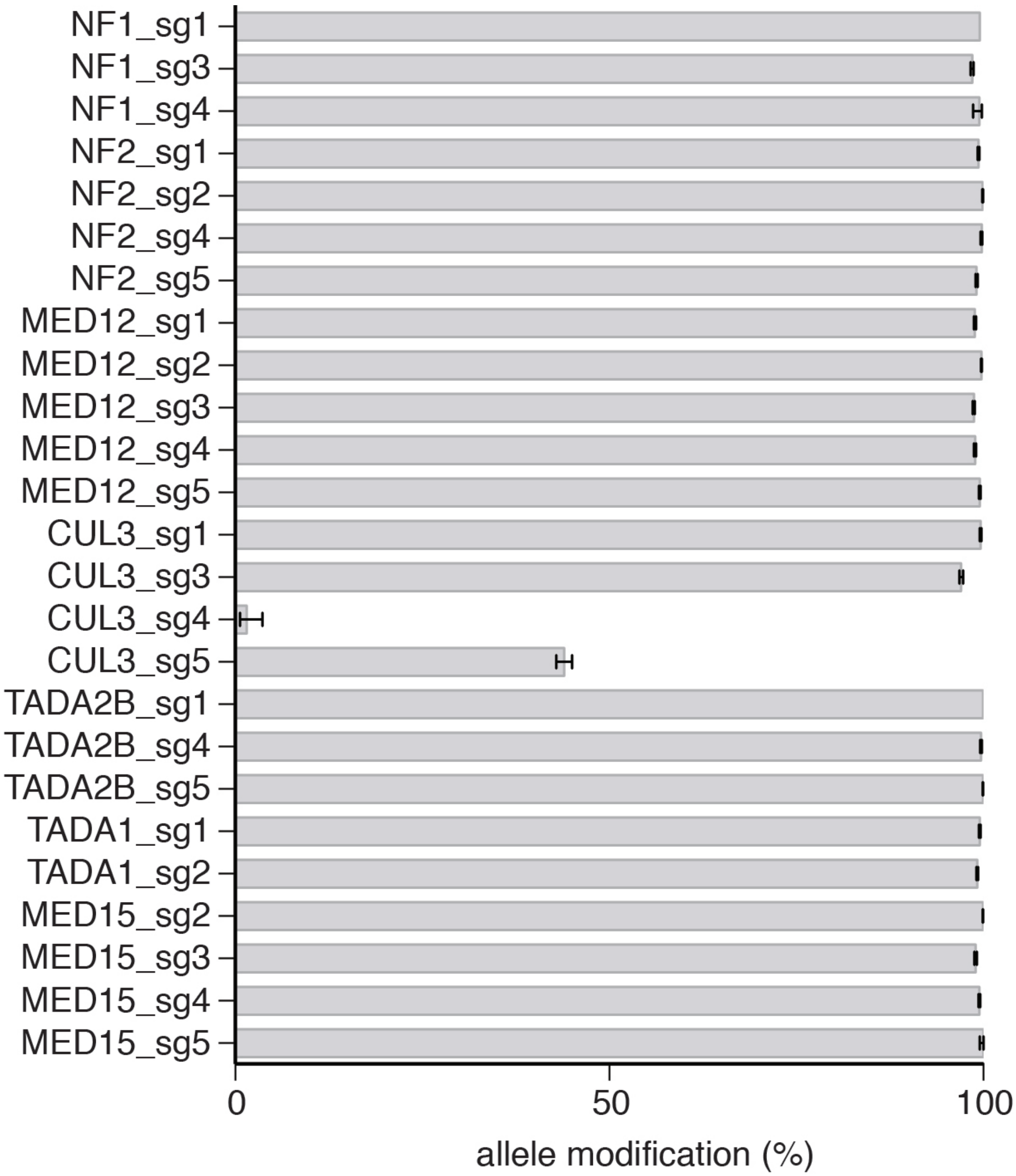

Fig. S12 | Measurements of allele modification frequencies in 25 sgRNAs targeting the seven highest-ranking genes in the A375 GeCKO screen

Bar plot shows the percentage of modified alleles determined by PCR followed by deep sequencing. Error bars representing Wilson intervals (as in (*35*)).

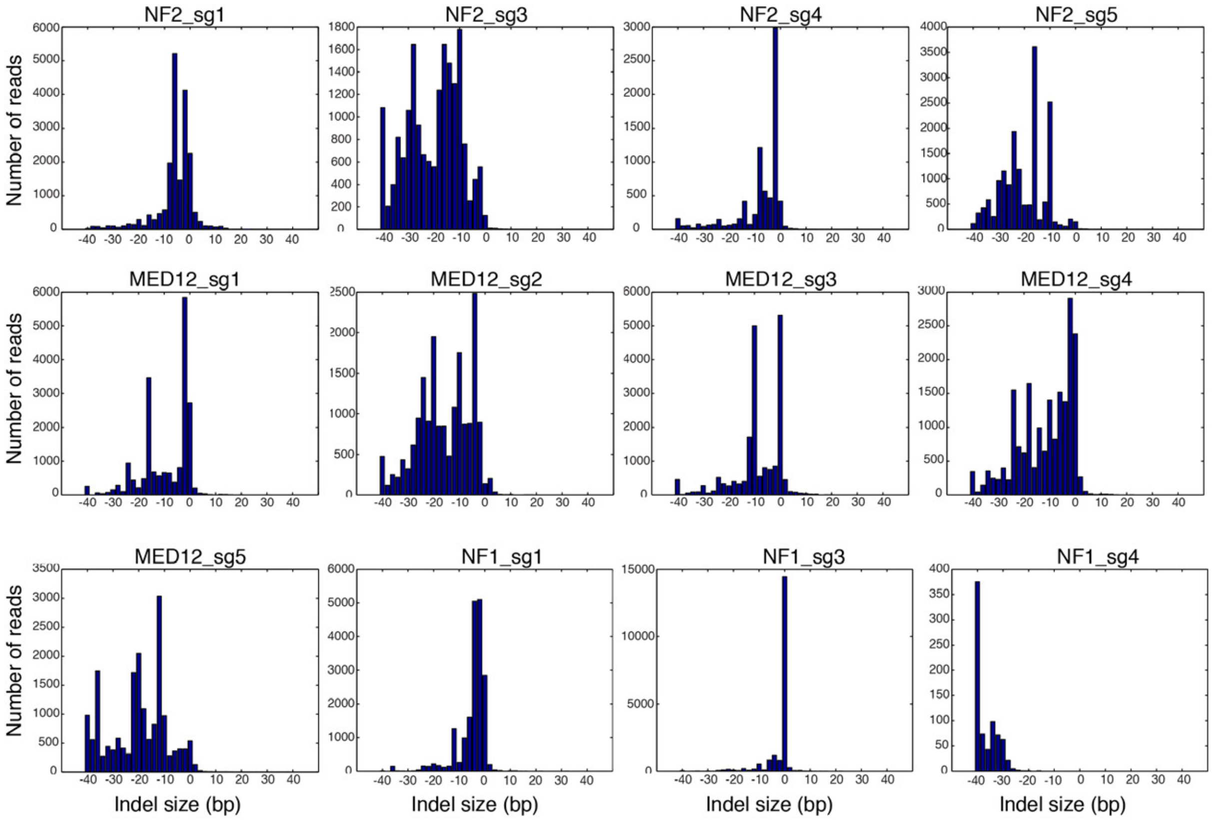

Fig. S13 | Histograms of on-target indel sizes for *NF2*, *MED12,* and *NF1*

Each subpanel shows the distribution of indel sizes for a single sgRNA at its intended genomic target locus. Each locus is PCR amplified and deep sequenced. Negative values indicate deletions and positive values indicate insertions.

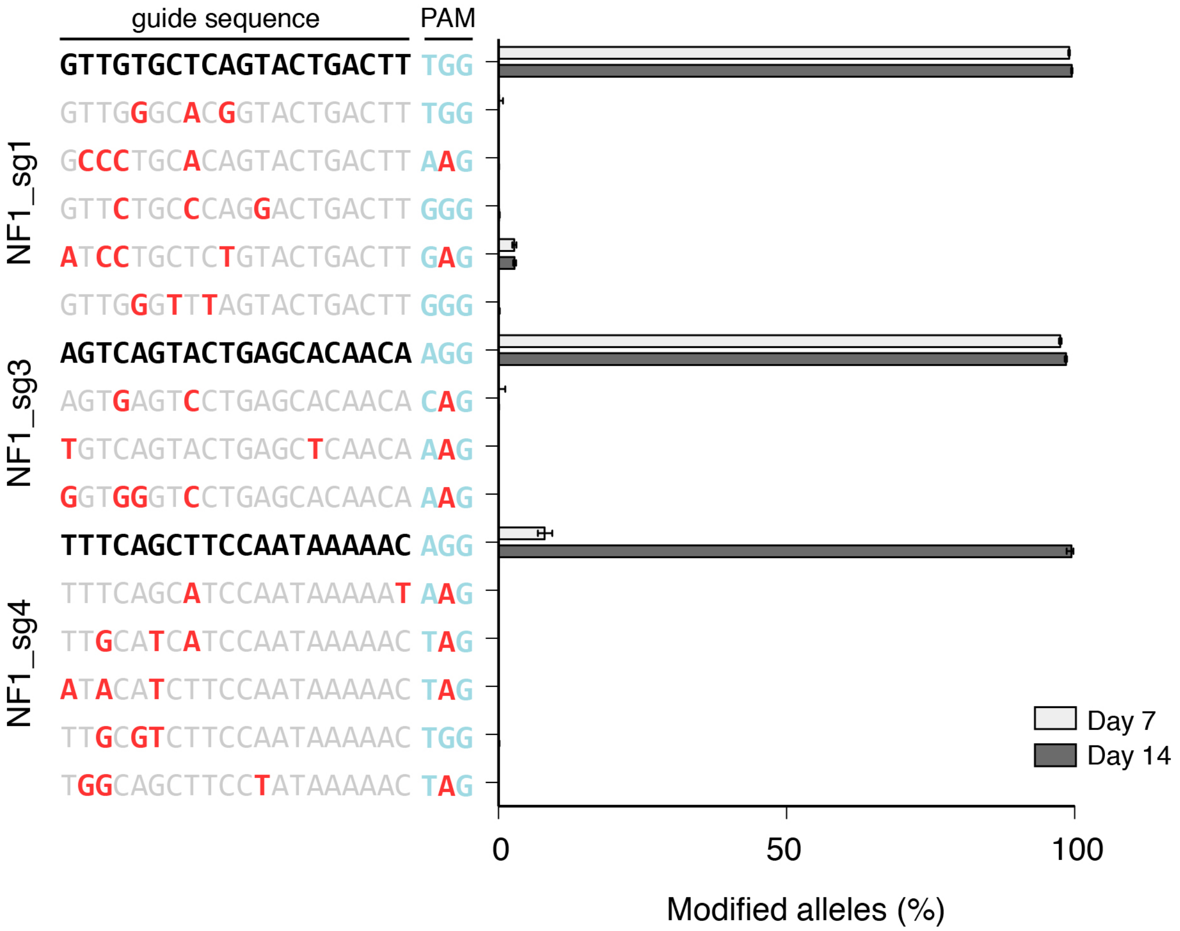

Fig. S14 | Measurements of on and off target allele modification frequencies for three sgRNAs targeting *NF1*

Each row represents a genomic locus consisting of a 20bp sgRNA site (in black or gray letters) followed by a 3bp PAM sequence (in light blue letters). Sequences in bold black letters indicate the genomic sequences that the GeCKO library sgRNAs were designed to target. Below each bold line are 3 to 5 predicted potential off target genomic sequences identified using the CRISPR design tool (http://tools.genome-engineering.org) (*37*). Red nucleotides highlight the differences in these off target sequences from the on target site. Each locus (on and off target) was PCR amplified and then deep sequenced. Bars show the percentage of modified alleles 7 and 14 days post transduction with error bars representing Wilson intervals (as in (*35*)).

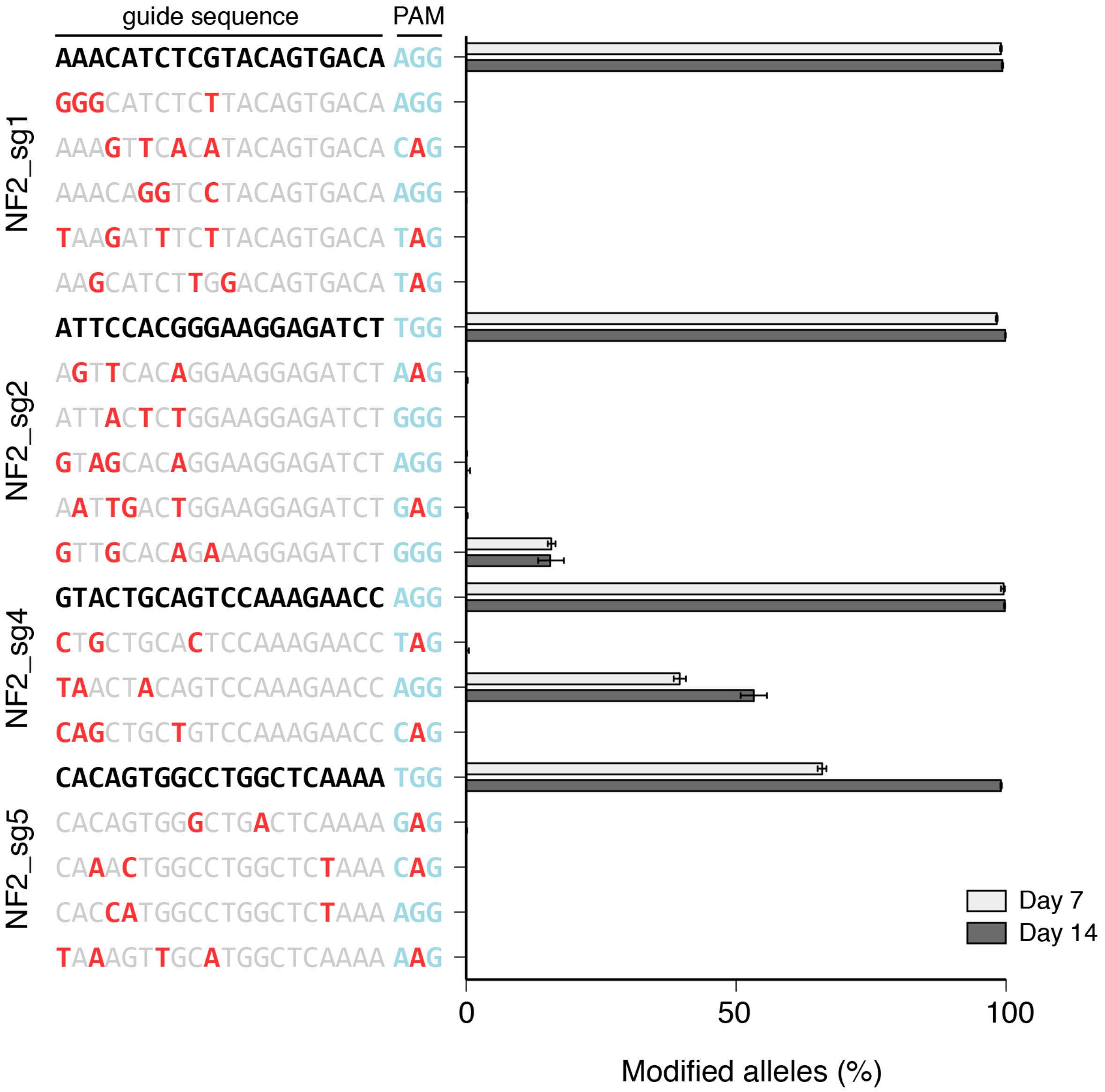

Fig. S15 | Measurements of on and off target allele modification frequencies for three sgRNAs targeting *NF2*

Each row represents a genomic locus consisting of a 20bp sgRNA site (in black or gray letters) followed by a 3bp PAM sequence (in light blue letters). Sequences in bold black letters indicate the genomic sequences that the GeCKO library sgRNAs were designed to target. Below each bold line are 3 to 5 predicted potential off target genomic sequences identified using the CRISPR design tool (http://tools.genome-engineering.org) (*37*). Red nucleotides highlight the differences in these off target sequences from the on target site. Each locus (on and off target) was PCR amplified and then deep sequenced. Bars show the percentage of modified alleles 7 and 14 days post transduction with error bars representing Wilson intervals (as in (*35*)).

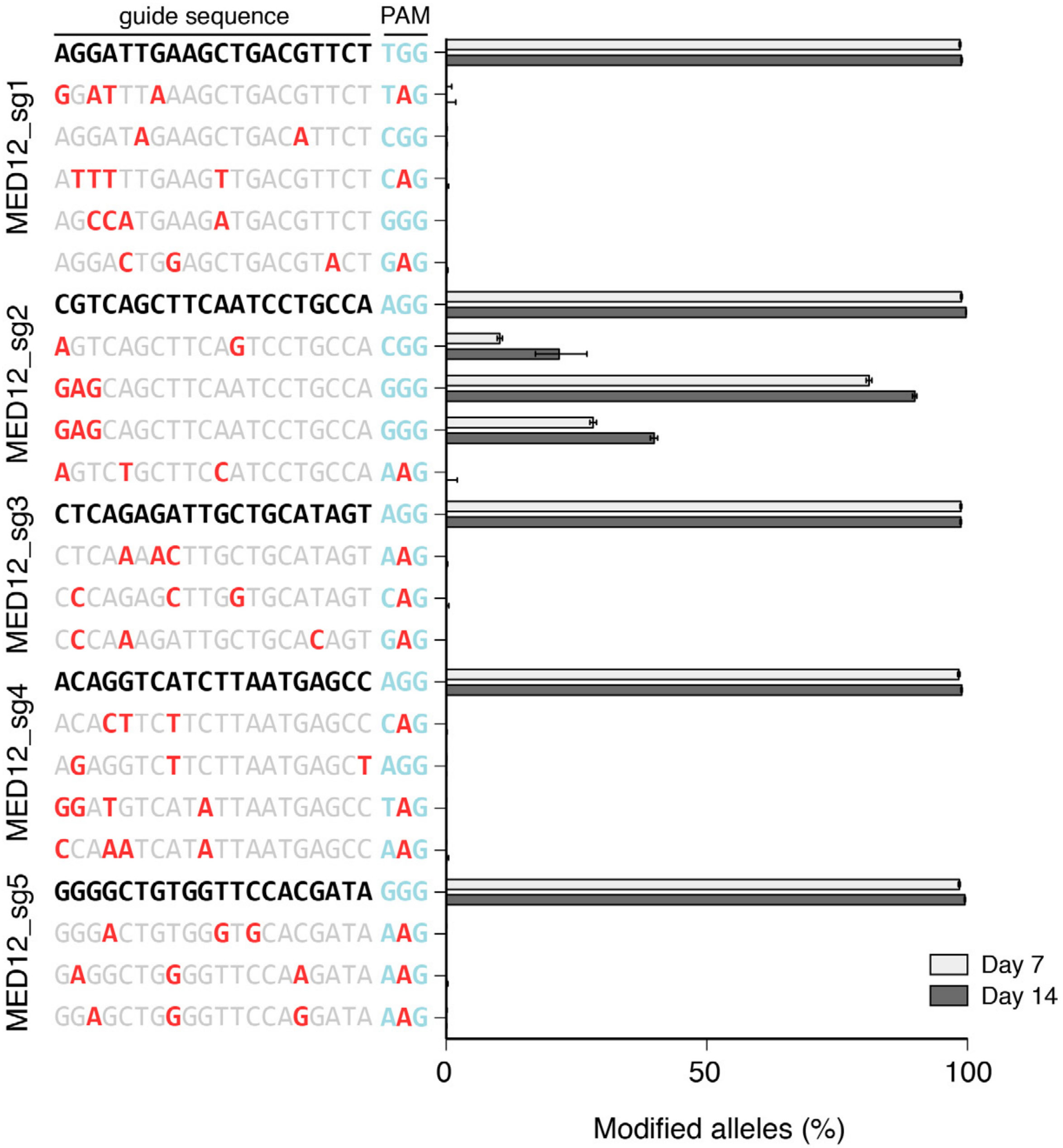

Fig. S16 | Measurements of on and off target allele modification frequencies for three sgRNAs targeting *MED12*

Each row represents a genomic locus consisting of a 20bp sgRNA site (in black or gray letters) followed by a 3bp PAM sequence (in light blue letters). Sequences in bold black letters indicate the genomic sequences that the GeCKO library sgRNAs were designed to target. Below each bold line are 3 to 5 predicted potential off target genomic sequences identified using the CRISPR design tool (http://tools.genome-engineering.org) (*37*). Red nucleotides highlight the differences in these off target sequences from the on target site. Each locus (on and off target) was PCR amplified and then deep sequenced. Bars show the percentage of modified alleles 7 and 14 days post transduction with error bars representing Wilson intervals (as in (*35*)).

SUPPLEMENTARY SEQUENCES

LentiCRISPR (pXPR_001 available through Addgene) *plasmid map & annotation key*

Pink	BsmBI TypeIIs sites for cloning in 20bp sgRNA guide sequence after removing 1.8kb spacer sequence
Green	+85 chRNA sequence for sgRNA
Gray	EFS promoter sequence
Yellow	Human codon-optimized SpCas9 coding sequence
Red	P2A bicistronic linker/self-cleaving peptide
Blue	Puromycin resistance coding sequence

Online plasmid map is available here: http://bit.ly/pLentiCRISPR

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GCTATGTGGCGCGGTATTATCCCGTATTGACGCCGGGCAAGAGCAACTCGGTCGCCGCATACAC
TATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCACAGAAAAGCATCTTACGGATGGCATGA
CAGTAAGAGAATTATGCAGTGCTGCCATAACCATGAGTGATAACACTGCGGCCAACTTACTTCT
GACAACGATCGGAGGACCGAAGGAGCTAACCGCTTTTTTGCACAACATGGGGGATCATGTAACT
CGCCTTGATCGTTGGGAACCGGAGCTGAATGAAGCCATACCAAACGACGAGCGTGACACCACGA
TGCCTGTAGCAATGGCAACAACGTTGCGCAAACTATTAACTGGCGAACTACTTACTCTAGCTTC
CCGGCAACAATTAATAGACTGGATGGAGGCGGATAAAGTTGCAGGACCACTTCTGCGCTCGGCC
CTTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGAGCCGGTGAGCGTGGGTCTCGCGGTATCA
TTGCAGCACTGGGGCCAGATGGTAAGCCCTCCCGTATCGTAGTTATCTACACGACGGGGAGTCA
GGCAACTATGGATGAACGAAATAGACAGATCGCTGAGATAGGTGCCTCACTGATTAAGCATTGG
TAACTGTCAGACCAAGTTTACTCATATATACTTTAGATTGATTTAAAACTTCATTTTTAATTTA
AAAGGATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAAAATCCCTTAACGTGAGTTTTC
GTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTTTTCTG
CGCGTAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGGTTTGTTTGCCGGATC
AAGAGCTACCAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACTGT
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GCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGGTTGG
ACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTGCACACA
GCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATACCTACAGCGTGAGCTATGAGAAAGC
GCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACAGGAG
AGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCCA
CCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAACGCC
AGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATGTTCTTTCCTG
CGTTATCCCCTGATTCTGTGGATAACCGTATTACCGCCTTTGAGTGAGCTGATACCGCTCGCCG
CAGCCGAACGACCGAGCGCAGCGAGTCAGTGAGCGAGGAAGCGGAAGAGCGCCCAATACGCAAA
CCGCCTCTCCCCGCGCGTTGGCCGATTCATTAATGCAGCTGGCACGACAGGTTTCCCGACTGGA
AAGCGGGCAGTGAGCGCAACGCAATTAATGTGAGTTAGCTCACTCATTAGGCACCCCAGGCTTT
ACACTTTATGCTTCCGGCTCGTATGTTGTGTGGAATTGTGAGCGGATAACAATTTCACACAGGA
AACAGCTATGACCATGATTACGCCAAGCGCGCAATTAACCCTCACTAAAGGGAACAAAAGCTGG
AGCTGCAAGC

Due to its large size, we were unable to upload **Table S1** via the Science Submission website. A PDF version is available online for download:

http://www.genome-engineering.org/papers/shalem2013/Table_S1.xlsx

All table captions are below with tables S2 to S6 following after the captions.

Table S1 | Database of 64,751 sgRNAs for GeCKO library with HUGO gene IDs, CCDS ID, and off-target (OS) score.

Table S2 | Gene Set Enrichment Analysis output for negative selection of essential genes in A375 cells after 14 additional days in culture. For the analysis, the *ALL Gene Ontology* set was used from the Moleular Signatures Database (MSigDB) with a minimum set size of 50 and max set size of 300.

Table S3 | Gene Set Enrichment Analysis output for negative selection of essential genes in HUES62 hES cells after 14 additional days in culture. For the analysis, the *ALL Gene Ontology* set was used from the Moleular Signatures Database (MSigDB) with a minimum set size of 50 and max set size of 300.

Table S4 | Top 1000 depleted genes for both A375 and HUES62. Mean depletion for each gene is given as the log2 ratio of Day 14 vs. Day 3 representation (mean over sgRNAs for the gene).

Table S5 | Output of the RIGER algorithm for the initial A375 PLX screen comparing PLX (mean of the two replicates at day 14) to vehicle control (mean of the two replicates at day 14). The weighted sum method was used to convert sgRNAs to genes. Genes are sorted by RIGER rank.

Table S6 | Output of the RIGER algorithm for the transduction replicate A375 PLX screen comparing PLX (mean of the two replicates at day 14) to vehicle control (mean of the two

replicates at day 14). The weighted sum method was used to convert sgRNAs to genes. Genes are sorted by RIGER rank.

Table S7 | Comparison of the top 20 hits between the two infection replicate screens by RIGER rank. The overlap of top hits between the two biological replicates with independent infections demonstrates the consistency of the GeCKO library.

Table S8 | Comparison of the top 20 hits between the two A375 PLX infection replicate screens by RSA rank. Redundant siRNA activity (RSA) uses an enrichment cutoff and hypergeometric test to measure the support for a gene using the enrichment of the sgRNAs (or shRNAs) for each gene.

Table S9 | Cas9-sgRNA array screening constructs used. Names and targeting sequence for all Cas9-sgRNA constructs used for validation in A375 screen. Cas9-sgRNAs with *names in italics* are contained in the GeCKO library.

Table S10 | shRNA array screening constructs used. Names and The RNAi Consortium (TRC) identification numbers for all shRNA constructs used for validation in A375 screen.

Table S2 | Gene Set Enrichment Analysis output for negative selection of essential genes in A375 cells after 14 additional days in culture. For the analysis, the *ALL Gene Ontology* set was used from the Moleular Signatures Database (MSigDB) with a minimum set size of 50 and max set size of 200.

NAME	SIZE	ES	NES	NOMp	FDRq	FWERp	RANK AT MAX
RNA_PROCESSING	169	0.45	6.78	0	0	0	4613
STRUCTURAL_CONSTITUENT_OF_RIBOSOME	76	0.63	6.48	0	0	0	4091
RIBONUCLEOPROTEIN_COMPLEX	141	0.43	6	0	0	0	3122
RNA_SPLICING	90	0.49	5.44	0	0	0	3166
RIBONUCLEOPROTEIN_COMPLEX_BIOGENESI	82	0.45	4.78	0	0	0	3300
MRNA_PROCESSING_GO_0006397	71	0.46	4.65	0	0	0	4504
MRNA_METABOLIC_PROCESS	81	0.44	4.62	0	0	0	5832
TRANSLATION	171	0.3	4.48	0	0	0	4605
SPLICEOSOME	50	0.53	4.42	0	0	0	3122
MITOCHONDRIAL_PART	138	0.31	4.14	0	0	0	5719
NUCLEOLUS	121	0.31	3.94	0	0	0	2989
CHROMOSOME	120	0.31	3.93	0	0	0	2562
CHROMOSOMAL_PART	94	0.34	3.81	0	0	0	4871
ORGANELLE_ENVELOPE	164	0.24	3.72	0	0	0	7637
ENVELOPE	164	0.24	3.64	0	0	0	7637
PROTEIN_RNA_COMPLEX_ASSEMBLY	63	0.39	3.63	0	0	0	3011
DNA_REPLICATION	99	0.31	3.63	0	0	0	3726
TRANSLATION_INITIATION_FACTOR_ACTIVITY	22	0.66	3.62	0	0	0	2922
RNA_SPLICINGVIA_TRANSESTERIFICATION_RI	34	0.52	3.6	0	0	0	4504
DNA_DIRECTED_RNA_POLYMERASEII_HOLOE	66	0.37	3.57	0	0	0	4378
TRANSLATION_FACTOR_ACTIVITY_NUCLEIC_	35	0.49	3.54	0	0	0	4020
ATP_DEPENDENT_HELICASE_ACTIVITY	27	0.57	3.52	0	0	0	3856
RIBOSOME	39	0.46	3.47	0	0	0	4679
TRANSLATION_REGULATOR_ACTIVITY	37	0.48	3.43	0	0	0	4020
HELICASE_ACTIVITY	50	0.41	3.39	0	0	0	4253
M_PHASE	113	0.27	3.38	0	0	0	3167
RNA_POLYMERASE_ACTIVITY	15	0.74	3.36	0	0	0	3534
MITOSIS	81	0.31	3.29	0	0	0	3167
M_PHASE_OF_MITOTIC_CELL_CYCLE	84	0.3	3.27	0	0	0	3167
TRANSCRIPTION_FACTOR_COMPLEX	89	0.29	3.24	0	0	0	7446
NUCLEOTIDYLTRANSFERASE_ACTIVITY	46	0.42	3.23	0	0	0	5034
MITOCHONDRIAL_ENVELOPE	93	0.28	3.15	0	0	0	7637
BIOPOLYMER_CATABOLIC_PROCESS	113	0.25	3.15	0	0	0	8133
MICROTUBULE_CYTOSKELETON	148	0.22	3.14	0	0	0	5149
ATP_DEPENDENT_RNA_HELICASE_ACTIVITY	17	0.63	3.13	0	0	0	3599
MITOCHONDRIAL_MATRIX	46	0.38	3.13	0	0	0	4866
MITOCHONDRIAL_MEMBRANE	82	0.29	3.13	0	0	0	5507
RRNA_METABOLIC_PROCESS	16	0.64	3.12	0	0	0	3132
MITOCHONDRIAL_INNER_MEMBRANE	64	0.32	3.09	0	0	0	5478
CELL_CYCLE_PROCESS	191	0.19	3.09	0	0	0	5108
MITOCHONDRIAL_LUMEN	46	0.38	3.05	0	0	0	4866
MITOCHONDRIAL_MEMBRANE_PART	50	0.36	3.04	0	0	0	6911
MACROMOLECULE_CATABOLIC_PROCESS	131	0.22	3.01	0	0	0	4410
ORGANELLE_INNER_MEMBRANE	72	0.3	3	0	0	0	7637
RNA_DEPENDENT_ATPASE_ACTIVITY	18	0.58	2.98	0	0	0	3599
CHROMOSOME_ORGANIZATION_AND_BIOG	124	0.23	2.97	0	0	0	7906
SMALL_NUCLEAR_RIBONUCLEOPROTEIN_CO	22	0.53	2.96	0	0	0	2790
RRNA_PROCESSING	15	0.63	2.92	0	0	0	3132
SPINDLE	37	0.4	2.9	0	2.11E-05	0.001	3082
NEGATIVE_REGULATION_OF_DNA_METABOL	18	0.56	2.89	0	2.07E-05	0.001	3927
NUCLEOLAR_PART	17	0.59	2.89	0	2.03E-05	0.001	5289
DNA_REPAIR	122	0.23	2.88	0	1.99E-05	0.001	8379
RIBOSOMAL_SUBUNIT	20	0.53	2.88	0	1.95E-05	0.001	7583
RIBOSOME_BIOGENESIS_AND_ASSEMBLY	17	0.59	2.88	0	1.92E-05	0.001	3132
CELLULAR_MACROMOLECULE_CATABOLIC_P	100	0.24	2.87	0	1.88E-05	0.001	4287
CELLULAR_PROTEIN_CATABOLIC_PROCESS	57	0.33	2.87	0	1.85E-05	0.001	3646
RESPONSE_TO_DNA_DAMAGE_STIMULUS	158	0.2	2.87	0	1.81E-05	0.001	8379
RNA_HELICASE_ACTIVITY	24	0.47	2.83	0	8.76E-05	0.005	4253
PROTEIN_CATABOLIC_PROCESS	67	0.3	2.82	0.002	8.61E-05	0.005	8133
CELL_CYCLE_PHASE	169	0.19	2.8	0	1.02E-04	0.006	6715
TRANSLATIONAL_INITIATION	36	0.4	2.8	0	1.18E-04	0.007	1821
SPINDLE_POLE	18	0.55	2.78	0	1.16E-04	0.007	3061
ENDONUCLEASE_ACTIVITY	25	0.45	2.75	0	1.30E-04	0.008	4802
RESPONSE_TO_ENDOGENOUS_STIMULUS	194	0.17	2.73	0	1.77E-04	0.011	9201
MITOCHONDRIAL_RIBOSOME	22	0.49	2.71	0	2.21E-04	0.014	7583
REPLICATION_FORK	17	0.54	2.71	0	2.18E-04	0.014	1946

DNA_DEPENDENT_DNA_REPLICATION	53	0.31	2.71	0	2.15E-04	0.014	3927
NUCLEAR_DNA_DIRECTED_RNA_POLYMERAS	17	0.53	2.69	0	2.72E-04	0.018	4181
MITOTIC_CELL_CYCLE	152	0.19	2.69	0	2.69E-04	0.018	5712
DNA_DIRECTED_RNA_POLYMERASE_COMPLE	17	0.53	2.69	0	2.79E-04	0.019	4181
ORGANELLAR_RIBOSOME	22	0.49	2.69	0	2.75E-04	0.019	7583
ATPASE_ACTIVITY	112	0.22	2.68	0	3.15E-04	0.022	8238
KINETOCHORE	24	0.45	2.67	0.002	3.53E-04	0.024	3167
MICROTUBULE_ORGANIZING_CENTER	65	0.28	2.65	0	3.63E-04	0.025	5750
CELLULAR_RESPIRATION	19	0.49	2.64	0	3.58E-04	0.025	5452
GENERAL_RNA_POLYMERASE_II_TRANSCRIPT	32	0.39	2.64	0	3.82E-04	0.027	4282
GOLGI_VESICLE_TRANSPORT	45	0.33	2.63	0	3.91E-04	0.028	3262
TRANSCRIPTION_INITIATION	35	0.37	2.63	0	3.86E-04	0.028	8749
RNA_POLYMERASE_COMPLEX	17	0.53	2.62	0	3.94E-04	0.029	4181
DOUBLE_STRAND_BREAK_REPAIR	23	0.45	2.61	0	4.02E-04	0.03	5933
CHROMOSOMEPERICENTRIC_REGION	30	0.4	2.61	0	3.97E-04	0.03	1862
NUCLEAR_PORE	31	0.4	2.58	0	4.80E-04	0.037	6200
TRANSCRIPTION_INITIATION_FROM_RNA_PC	29	0.4	2.57	0	5.37E-04	0.042	8296
ATPASE_ACTIVITY_COUPLED	93	0.23	2.56	0	6.43E-04	0.051	6313
PROTEIN_DNA_COMPLEX_ASSEMBLY	48	0.31	2.56	0	6.35E-04	0.051	8352
REGULATION_OF_DNA_METABOLIC_PROCES	45	0.32	2.54	0	6.89E-04	0.056	3927
NUCLEAR_MEMBRANE_PART	42	0.33	2.53	0	7.42E-04	0.061	7889
TRANSCRIPTION_FROM_RNA_POLYMERASE_	19	0.49	2.52	0	7.80E-04	0.065	5433
CONDENSED_CHROMOSOME	33	0.37	2.5	0	8.85E-04	0.074	2562
DNA_INTEGRITY_CHECKPOINT	23	0.44	2.5	0	8.86E-04	0.075	3927
NUCLEASE_ACTIVITY	55	0.28	2.49	0	9.23E-04	0.079	4802
PROTEASOME_COMPLEX	23	0.43	2.47	0	0.0010595	0.09	3950
CELL_CYCLE_CHECKPOINT_GO_0000075	47	0.3	2.45	0	0.0011911	0.101	6812
SPLICEOSOME_ASSEMBLY	21	0.44	2.44	0	0.0012657	0.109	5832
PROTEIN_FOLDING	56	0.27	2.42	0	0.001526	0.132	10933
CENTROSOME	56	0.27	2.41	0	0.0017435	0.152	5750
REGULATION_OF_CELL_CYCLE	177	0.15	2.39	0.002	0.0019596	0.172	3790
PORE_COMPLEX	36	0.33	2.39	0	0.0019396	0.172	6580
RNA_EXPORT_FROM_NUCLEUS	20	0.45	2.38	0	0.002034	0.182	3599
AEROBIC_RESPIRATION	15	0.5	2.35	0	0.0024926	0.218	5452
DNA_HELICASE_ACTIVITY	24	0.41	2.32	0	0.0029406	0.255	7740
LIGASE_ACTIVITY	94	0.21	2.32	0	0.0030217	0.263	4553
ESTABLISHMENT_AND_OR_MAINTENANCE_C	77	0.22	2.31	0	0.003114	0.273	7475
RIBONUCLEASE_ACTIVITY	25	0.4	2.31	0	0.0032127	0.285	4435
CHROMATIN_MODIFICATION	55	0.26	2.31	0.002	0.0031927	0.286	7446
NUCLEOBASENUCLEOSIDENUCLEOTIDE_AND_	31	0.35	2.29	0	0.0035496	0.317	3657
DNA_DEPENDENT_ATPASE_ACTIVITY	22	0.41	2.28	0	0.0035659	0.32	5771
REGULATION_OF_TRANSLATIONAL_INITIATIC	28	0.36	2.25	0	0.004431	0.381	1821
ENERGY_DERIVATION_BY_OXIDATION_OF_O	36	0.32	2.25	0	0.0044668	0.388	6765
MICROTUBULE	30	0.34	2.23	0.002	0.0053178	0.442	7786
NUCLEAR_ENVELOPE	72	0.22	2.21	0.002	0.005955	0.477	6338
RNA_SPLICING_FACTOR_ACTIVITYTRANSESTE	19	0.42	2.2	0	0.0060397	0.481	8647
LIGASE_ACTIVITY_FORMING_CARBON_NITRC	67	0.23	2.18	0.002	0.0067538	0.528	8275
PROTEIN_TRANSPORT	152	0.15	2.16	0	0.0077929	0.574	6719
ACID_AMINO_ACID_LIGASE_ACTIVITY	57	0.24	2.13	0.002	0.0094787	0.646	8104
RIBONUCLEOTIDE_METABOLIC_PROCESS	15	0.45	2.11	0	0.0107778	0.698	5094
PROTON_TRANSPORTING_TWO_SECTOR_ATI	15	0.44	2.09	0.002	0.0119253	0.736	5367
MICROTUBULE_CYTOSKELETON_ORGANIZATI	33	0.3	2.08	0.006	0.0128761	0.764	2742
DNA_RECOMBINATION	47	0.25	2.06	0.002	0.0141296	0.796	2870
NUCLEAR_MEMBRANE	50	0.25	2.06	0	0.0140885	0.8	6338
INTRACELLULAR_PROTEIN_TRANSPORT	141	0.15	2.05	0	0.0149136	0.827	4528
ESTABLISHMENT_OF_PROTEIN_LOCALIZATIO	185	0.13	2.05	0.004	0.0152041	0.833	7338
MRNA_BINDING	22	0.37	2.03	0.004	0.017169	0.872	6415
MITOTIC_SISTER_CHROMATID_SEGREGATION	16	0.42	2.02	0	0.0172391	0.875	1498
PROTEIN_MODIFICATION_BY_SMALL_PROTE	43	0.26	2.02	0.004	0.0172653	0.877	8688
SMALL_CONJUGATING_PROTEIN_LIGASE_AC	51	0.24	2.01	0.008	0.0184011	0.897	8104
CHROMOSOME_SEGREGATION	32	0.3	2.01	0.004	0.0185071	0.901	1862
MICROTUBULE_ORGANIZING_CENTER_PART	19	0.38	2	0.002	0.0195922	0.91	3621
PROTEIN_TARGETING	108	0.16	1.97	0.004	0.0228002	0.932	5629
PHOSPHATASE_REGULATOR_ACTIVITY	25	0.32	1.96	0.008	0.0236637	0.943	4330
EXONUCLEASE_ACTIVITY	19	0.38	1.96	0	0.0238019	0.945	3623
NUCLEAR_EXPORT	33	0.29	1.96	0.006	0.0239499	0.946	3599
DNA_DAMAGE_CHECKPOINT	19	0.36	1.94	0.006	0.0271678	0.967	3927
SISTER_CHROMATID_SEGREGATION	17	0.39	1.93	0.008	0.0281053	0.97	1498
NUCLEAR_CHROMOSOME	52	0.23	1.92	0.004	0.0292856	0.977	4966
NUCLEAR_TRANSPORT	86	0.18	1.91	0.01	0.0302563	0.981	3785
REGULATION_OF_MITOSIS	40	0.26	1.91	0.01	0.0305927	0.981	1262

MEDIATOR_COMPLEX	18	0.38	1.91	0.008	0.0306269	0.982	2201
SMALL_PROTEIN_CONJUGATING_ENZYME_A	52	0.23	1.9	0.01	0.0316691	0.985	8104
TUBULIN_BINDING	45	0.24	1.89	0.011	0.034726	0.99	2562
GOLGI_APPARATUS_PART	96	0.16	1.87	0.004	0.0376059	0.995	5627
PHOSPHOTRANSFERASE_ACTIVITY_PHOSPHA	18	0.36	1.87	0.008	0.037624	0.995	3501
MONOVALENT_INORGANIC_CATION_TRANS	33	0.27	1.86	0.006	0.0382074	0.996	8238
ORGANELLE_LOCALIZATION	24	0.31	1.86	0.018	0.0385921	0.997	1862
MEIOTIC_CELL_CYCLE	35	0.27	1.86	0.014	0.0388517	0.997	2870
UBIQUITIN_PROTEIN_LIGASE_ACTIVITY	49	0.23	1.85	0.01	0.0390875	0.997	8104
UBIQUITIN_CYCLE	48	0.23	1.85	0.01	0.039222	0.998	5352
HISTONE_ACETYLTRANSFERASE_ACTIVITY	16	0.38	1.84	0.018	0.0420917	0.998	4521
PROTEIN_UBIQUITINATION	40	0.24	1.83	0.017	0.0433416	0.998	8688
ER_TO_GOLGI_VESICLE_MEDIATED_TRANSP	17	0.37	1.83	0.012	0.043888	0.998	2904
DAMAGED_DNA_BINDING	20	0.34	1.83	0.022	0.0440346	0.998	7435
REGULATION_OF_CELLULAR_COMPONENT_	118	0.14	1.83	0.008	0.0440416	0.998	6048
NUCLEOCYTOPLASMIC_TRANSPORT	85	0.17	1.83	0.021	0.0438203	0.998	3785
ACETYLTRANSFERASE_ACTIVITY	25	0.3	1.82	0.012	0.0437303	0.998	8277
REGULATION_OF_DNA_REPLICATION	20	0.33	1.81	0.015	0.0460174	0.999	3927
MITOCHONDRION_ORGANIZATION_AND_BI	46	0.22	1.8	0.014	0.048121	1	6208
MITOCHONDRIAL_RESPIRATORY_CHAIN	23	0.32	1.8	0.015	0.049284	1	5274
DNA_REPLICATION_INITIATION	15	0.38	1.8	0.013	0.0501737	1	3927
GUANYL_NUCLEOTIDE_EXCHANGE_FACTOR_	46	0.22	1.79	0.018	0.0523188	1	9698
NUCLEOBASENUCLEOSIDE_AND_NUCLEOTID	51	0.21	1.78	0.027	0.0529904	1	5094
DNA_POLYMERASE_ACTIVITY	18	0.34	1.78	0.018	0.0526805	1	7868
UNFOLDED_PROTEIN_BINDING	41	0.23	1.77	0.022	0.0558528	1	4703
CHROMATIN_REMODELING	25	0.29	1.77	0.014	0.0564238	1	5533
TRANSCRIPTION_ACTIVATOR_ACTIVITY	172	0.12	1.76	0.025	0.05713	1	3647
PROTEIN_AMINO_ACID_N_LINKED_GLYCOSY	30	0.27	1.76	0.026	0.0572967	1	4758
ESTABLISHMENT_OF_ORGANELLE_LOCALIZA	18	0.34	1.76	0.032	0.0584708	1	1862
GLUCOSE_METABOLIC_PROCESS	28	0.28	1.74	0.01	0.0625718	1	5300
NUCLEOTIDE_BIOSYNTHETIC_PROCESS	19	0.34	1.74	0.02	0.063041	1	10047
TRANSFERASE_ACTIVITY_TRANSFERRING_AL	28	0.27	1.73	0.018	0.0657584	1	9270
RESPONSE_TO_ORGANIC_SUBSTANCE	29	0.27	1.72	0.025	0.0690078	1	10758
CONDENSED_NUCLEAR_CHROMOSOME	18	0.34	1.71	0.03	0.0722966	1	4966
CYTOKINESIS	18	0.34	1.71	0.032	0.0730998	1	7906
APOPTOTIC_NUCLEAR_CHANGES	18	0.33	1.71	0.03	0.0736285	1	6024
N_ACYLTRANSFERASE_ACTIVITY	24	0.29	1.71	0.02	0.0732113	1	8277
HISTONE_MODIFICATION	24	0.29	1.7	0.026	0.0738421	1	9842
INOSITOL_OR_PHOSPHATIDYLINOSITOL_KIN	18	0.33	1.7	0.031	0.0744174	1	6087
TRANSCRIPTION_COACTIVATOR_ACTIVITY	122	0.13	1.7	0.025	0.0742021	1	8574
NUCLEAR_CHROMOSOME_PART	33	0.25	1.69	0.02	0.0770794	1	4871
SINGLE_STRANDED_DNA_BINDING	33	0.25	1.68	0.035	0.0812054	1	2691
STRUCTURE_SPECIFIC_DNA_BINDING	54	0.19	1.67	0.029	0.0830904	1	2870
COFACTOR_METABOLIC_PROCESS	54	0.19	1.67	0.032	0.0833364	1	8590
PROTEIN_C_TERMINUS_BINDING	70	0.17	1.67	0.038	0.0847242	1	6814
INTRINSIC_TO_ORGANELLE_MEMBRANE	51	0.2	1.67	0.04	0.0848346	1	7012
GTP_BINDING	43	0.21	1.66	0.036	0.0874981	1	5872
N_ACETYLTRANSFERASE_ACTIVITY	21	0.3	1.65	0.033	0.0897944	1	8277
POSITIVE_REGULATION_OF_PHOSPHORYLAT	26	0.27	1.65	0.03	0.0900264	1	5576
PROTEIN_AMINO_ACID_LIPIDATION	23	0.29	1.64	0.039	0.0943972	1	4958
PROTEIN_IMPORT	62	0.18	1.64	0.043	0.0948416	1	6719
PEPTIDYL_AMINO_ACID_MODIFICATION	63	0.18	1.63	0.032	0.0968288	1	4587
CELLULAR_COMPONENT_DISASSEMBLY	32	0.24	1.63	0.028	0.0967863	1	8054
NUCLEAR_BODY	31	0.25	1.63	0.031	0.0972644	1	2564
INTRINSIC_TO_GOLGI_MEMBRANE	15	0.35	1.62	0.037	0.0988538	1	7012
MEIOTIC_RECOMBINATION	17	0.33	1.62	0.045	0.0984278	1	3623
POSITIVE_REGULATION_OF_PROTEIN_MODI	29	0.24	1.62	0.03	0.1023242	1	4931
REGULATION_OF_PROTEIN_METABOLIC_PR	167	0.11	1.61	0.034	0.1026857	1	8021
HYDROGEN_ION_TRANSMEMBRANE_TRANS	27	0.26	1.61	0.045	0.1024094	1	5274
MICROTUBULE_BINDING	31	0.25	1.61	0.049	0.1048693	1	2562
MICROTUBULE_BASED_PROCESS	79	0.15	1.6	0.034	0.1055417	1	2742
RAS_GUANYL_NUCLEOTIDE_EXCHANGE_FACT	19	0.31	1.6	0.052	0.1076924	1	8746
REGULATION_OF_CYCLIN_DEPENDENT_PROT	42	0.21	1.6	0.045	0.1086744	1	5698
CHROMATIN	35	0.23	1.59	0.037	0.1106927	1	4150
INTEGRAL_TO_ORGANELLE_MEMBRANE	49	0.18	1.58	0.057	0.113723	1	7012
MACROMOLECULAR_COMPLEX_DISASSEMBL	15	0.33	1.58	0.048	0.1132282	1	7211
UBIQUITIN_LIGASE_COMPLEX	26	0.26	1.58	0.049	0.1140445	1	5022
COFACTOR_BIOSYNTHETIC_PROCESS	21	0.29	1.58	0.054	0.1142278	1	8590
RNA_POLYMERASE_II_TRANSCRIPTION_FACT	181	0.1	1.58	0.047	0.1152211	1	4282
INORGANIC_CATION_TRANSMEMBRANE_TR	57	0.18	1.58	0.041	0.1152133	1	8238
SECRETORY_PATHWAY	81	0.15	1.57	0.06	0.1200102	1	3366

GTPASE_REGULATOR_ACTIVITY	123	0.12	1.57	0.052	0.1195898	1	11955
ISOMERASE_ACTIVITY	35	0.22	1.56	0.053	0.1208903	1	9450
RNA_CATABOLIC_PROCESS	22	0.28	1.56	0.058	0.1207908	1	10547
GUANYL_NUCLEOTIDE_BINDING	44	0.2	1.56	0.056	0.1204475	1	5872
HISTONE_DEACETYLASE_COMPLEX	20	0.29	1.55	0.05	0.1250101	1	7446
NUCLEOTIDE_EXCISION_REPAIR	20	0.28	1.55	0.036	0.1247534	1	9378
TRNA_METABOLIC_PROCESS	18	0.3	1.51	0.065	0.147658	1	4613
POSITIVE_REGULATION_OF_TRANSCRIPTIONI	118	0.12	1.51	0.046	0.1499894	1	11629
POSITIVE_REGULATION_OF_RNA_METABOLI	120	0.12	1.51	0.079	0.1513111	1	7400
GOLGI_MEMBRANE	43	0.19	1.5	0.069	0.1520378	1	7012
LIPOPROTEIN_BIOSYNTHETIC_PROCESS	25	0.25	1.5	0.071	0.1551175	1	4958
COVALENT_CHROMATIN_MODIFICATION	25	0.26	1.49	0.083	0.1590121	1	9842
POSITIVE_REGULATION_OF_PROTEIN_AMIN	20	0.28	1.49	0.063	0.16183	1	4931
ALCOHOL_METABOLIC_PROCESS	87	0.13	1.48	0.085	0.1646471	1	4869
MONOOXYGENASE_ACTIVITY	29	0.23	1.46	0.066	0.1776193	1	12143
ER_GOLGI_INTERMEDIATE_COMPARTMENT	24	0.25	1.46	0.07	0.1783043	1	7619
PHOSPHOINOSITIDE_METABOLIC_PROCESS	30	0.23	1.46	0.094	0.1799774	1	4958
SEQUENCE_SPECIFIC_DNA_BINDING	57	0.16	1.46	0.081	0.1807312	1	10388
NUCLEOTIDE_METABOLIC_PROCESS	41	0.19	1.45	0.085	0.1833199	1	8003
RESPONSE_TO_UV	25	0.24	1.45	0.082	0.183231	1	7960
COENZYME_METABOLIC_PROCESS	38	0.19	1.45	0.088	0.1842118	1	5094
POSITIVE_REGULATION_OF_PHOSPHATE_ME	28	0.23	1.45	0.085	0.1835406	1	5576
MITOTIC_CELL_CYCLE_CHECKPOINT	21	0.26	1.45	0.1	0.1853211	1	1262
REGULATION_OF_TRANSLATION	90	0.13	1.45	0.066	0.1855509	1	1837
DEOXYRIBONUCLEASE_ACTIVITY	22	0.25	1.44	0.091	0.1901669	1	3623
PHOSPHOINOSITIDE_BIOSYNTHETIC_PROCES	23	0.25	1.44	0.085	0.1899773	1	4958
NUCLEAR_ENVELOPE_ENDOPLASMIC_RETICU	91	0.13	1.41	0.098	0.2141808	1	3432
ENDOPLASMIC_RETICULUM_MEMBRANE	82	0.13	1.4	0.088	0.2161597	1	6659
REGULATION_OF_CELLULAR_PROTEIN_META	157	0.09	1.39	0.116	0.2269037	1	6135
CELL_DIVISION	20	0.26	1.39	0.106	0.2278685	1	7906
PROTEIN_N_TERMINUS_BINDING	37	0.19	1.39	0.117	0.2290458	1	6812
MEIOSIS_I	20	0.27	1.39	0.107	0.2283077	1	6056
POSITIVE_REGULATION_OF_TRANSCRIPTION	144	0.1	1.38	0.125	0.2340024	1	11633
REGULATION_OF_PROTEIN_MODIFICATION_	44	0.17	1.37	0.124	0.2424216	1	8816
POSITIVE_REGULATION_OF_NUCLEOBASENU	154	0.09	1.37	0.127	0.2439105	1	12302
PEROXISOME_ORGANIZATION_AND_BIOGEN	16	0.28	1.36	0.12	0.2473082	1	7338
PROTEOLYSIS	184	0.09	1.35	0.124	0.2585939	1	9188
MEMBRANE_COAT	15	0.29	1.35	0.129	0.257766	1	5576
REGULATION_OF_CATABOLIC_PROCESS	16	0.28	1.35	0.132	0.2596395	1	10771
DNA_CATABOLIC_PROCESS	22	0.24	1.35	0.136	0.2591224	1	8054
ACTIN_FILAMENT_BINDING	25	0.22	1.35	0.133	0.2599459	1	6814
POSITIVE_REGULATION_OF_I_KAPPAB_KINA	85	0.12	1.34	0.145	0.2612431	1	10774
COATED_MEMBRANE	15	0.29	1.34	0.149	0.2605071	1	5576
REGULATION_OF_PHOSPHORYLATION	48	0.16	1.34	0.145	0.2638062	1	5712
TRANSFERASE_ACTIVITY_TRANSFERRING_GR	49	0.16	1.34	0.143	0.2646159	1	4521
MICROTUBULE_ORGANIZING_CENTER_ORGA	15	0.29	1.34	0.147	0.2639838	1	5643
SMALL_GTPASE_REGULATOR_ACTIVITY	67	0.14	1.33	0.14	0.2649767	1	14777
ESTABLISHMENT_AND_OR_MAINTENANCE_	17	0.26	1.32	0.155	0.2755683	1	11192
RESPONSE_TO_HORMONE_STIMULUS	32	0.2	1.32	0.164	0.2799171	1	4309
NUCLEAR_IMPORT	49	0.16	1.32	0.149	0.2816584	1	6719
DNA_DAMAGE_RESPONSESIGNAL_TRANSDU	34	0.19	1.31	0.156	0.2864835	1	2504
ENZYME_BINDING	174	0.09	1.31	0.145	0.2854842	1	8331
CHROMATIN_BINDING	32	0.19	1.3	0.136	0.2934912	1	4966
METHYLTRANSFERASE_ACTIVITY	36	0.18	1.29	0.158	0.3028419	1	3724
GENERATION_OF_PRECURSOR_METABOLITE	122	0.1	1.29	0.175	0.3051191	1	7856
CHROMATIN_ASSEMBLY_OR_DISASSEMBLY	26	0.21	1.29	0.171	0.3083173	1	8772
TRANS_GOLGI_NETWORK	21	0.24	1.28	0.185	0.3135859	1	11201
TRANSFERASE_ACTIVITY_TRANSFERRING_ON	37	0.17	1.28	0.175	0.3127476	1	1743
MITOCHONDRIAL_TRANSPORT	20	0.24	1.27	0.196	0.3285474	1	3857
COATED_VESICLE_MEMBRANE	15	0.27	1.26	0.198	0.3366046	1	1196
INTERPHASE_OF_MITOTIC_CELL_CYCLE	62	0.14	1.25	0.184	0.3430329	1	6300
PROTEIN_HETERODIMERIZATION_ACTIVITY	76	0.12	1.25	0.192	0.3461332	1	8789
MITOCHONDRIAL_OUTER_MEMBRANE	17	0.25	1.24	0.175	0.35391	1	2882
CARBOHYDRATE_KINASE_ACTIVITY	15	0.26	1.24	0.217	0.3531388	1	10960
NUCLEOBASENUCLEOSIDENUCLEOTIDE_KINA	25	0.21	1.24	0.208	0.3522619	1	4198
LEADING_EDGE	47	0.15	1.24	0.186	0.3547705	1	5769
REGULATION_OF_PROTEIN_AMINO_ACID_P	30	0.19	1.24	0.204	0.3575871	1	5576
MICROTUBULE_ASSOCIATED_COMPLEX	46	0.15	1.23	0.178	0.3573947	1	5108
SECRETION_BY_CELL	113	0.1	1.23	0.205	0.3647618	1	3491
PROTEIN_IMPORT_INTO_NUCLEUS	48	0.15	1.22	0.233	0.3678567	1	6719
SH2_DOMAIN_BINDING	15	0.26	1.22	0.215	0.3685336	1	7291

ENDOPLASMIC_RETICULUM_PART	93	0.11	1.22	0.207	0.3708213	1	7200
TRANSFERASE_ACTIVITY_TRANSFERRING_ACY	59	0.13	1.21	0.229	0.3811329	1	2819
REGULATION_OF_PROTEIN_STABILITY	19	0.23	1.21	0.241	0.3874862	1	5364
PROTEIN_COMPLEX_ASSEMBLY	162	0.08	1.2	0.244	0.3929992	1	5785
PIGMENT_BIOSYNTHETIC_PROCESS	17	0.25	1.2	0.24	0.396801	1	7250
INTERPHASE	68	0.12	1.2	0.244	0.3979042	1	6300
ENDOSOME_TRANSPORT	23	0.21	1.19	0.255	0.4020253	1	11122
GOLGI_ASSOCIATED_VESICLE	27	0.19	1.19	0.234	0.4073514	1	3262
CHLORIDE_CHANNEL_ACTIVITY	19	0.23	1.19	0.25	0.4071226	1	8262
PHAGOCYTOSIS	16	0.24	1.19	0.244	0.4059333	1	13703
GLYCOPROTEIN_BIOSYNTHETIC_PROCESS	74	0.12	1.18	0.239	0.4079241	1	10136
PROTEIN_PROCESSING	48	0.14	1.18	0.248	0.4076695	1	10976
PHOSPHORIC_ESTER_HYDROLASE_ACTIVITY	149	0.08	1.18	0.225	0.4082036	1	13811
RESPONSE_TO_TEMPERATURE_STIMULUS	15	0.25	1.18	0.261	0.4127545	1	1535
CELLULAR_PROTEIN_COMPLEX_ASSEMBLY	32	0.17	1.18	0.243	0.412146	1	5899
RESPONSE_TO_BIOTIC_STIMULUS	114	0.09	1.18	0.247	0.4121309	1	13860
REGULATION_OF_I_KAPPAB_KINASE_NF_KAP	91	0.11	1.17	0.25	0.4179176	1	10774
THYROID_HORMONE_RECEPTOR_BINDING	17	0.23	1.16	0.264	0.4258486	1	4282
RESPONSE_TO_ABIOTIC_STIMULUS	83	0.11	1.16	0.271	0.4287692	1	11536
HORMONE_RECEPTOR_BINDING	29	0.18	1.16	0.284	0.4284073	1	4861
ENZYME_ACTIVATOR_ACTIVITY	120	0.09	1.16	0.261	0.4336155	1	14520
MEMBRANE_LIPID_BIOSYNTHETIC_PROCESS	48	0.14	1.15	0.276	0.438411	1	5034
RESPONSE_TO_BACTERIUM	29	0.18	1.14	0.263	0.4510156	1	13611
VESICLE_MEDIATED_TRANSPORT	189	0.07	1.13	0.291	0.4622929	1	15959
RAS_PROTEIN_SIGNAL_TRANSDUCTION	65	0.12	1.13	0.305	0.4656126	1	9838
ANION_CATION_SYMPORTER_ACTIVITY	16	0.24	1.13	0.288	0.4648375	1	12649
POSITIVE_REGULATION_OF_PROTEIN_METAB	74	0.11	1.13	0.291	0.4684199	1	8996
KINASE_BINDING	68	0.12	1.13	0.286	0.4674736	1	11445
POSITIVE_REGULATION_OF_TRANSCRIPTION_	65	0.12	1.12	0.292	0.4705558	1	4282
INTRAMOLECULAR_OXIDOREDUCTASE_ACTIV	19	0.21	1.12	0.31	0.4718874	1	2895
CELL_SUBSTRATE_ADHESION	38	0.15	1.12	0.289	0.4737092	1	9143
ACTIN_BINDING	76	0.11	1.11	0.308	0.4786494	1	9473
RUFFLE	31	0.17	1.11	0.305	0.4773997	1	5769
INDUCTION_OF_APOPTOSIS_BY_EXTRACELLU	25	0.19	1.11	0.32	0.4765128	1	11068
COATED_VESICLE	43	0.14	1.11	0.315	0.4854083	1	8368
TRANSFERASE_ACTIVITY_TRANSFERRING_HEX	80	0.11	1.1	0.327	0.4916188	1	10065
REGULATION_OF_CELL_MIGRATION	28	0.17	1.09	0.337	0.5018703	1	11741
ATPASE_ACTIVITY_COUPLED_TO_TRANSMEM	24	0.18	1.09	0.33	0.5043768	1	13241
LIPID_TRANSPORTER_ACTIVITY	28	0.17	1.09	0.339	0.5051969	1	12367
PROTEIN_AMINO_ACID_AUTOPHOSPHORYLA	30	0.17	1.09	0.356	0.5064648	1	10204
FEEDING_BEHAVIOR	24	0.19	1.08	0.357	0.5136158	1	13940
TRANSFERASE_ACTIVITY_TRANSFERRING_GLY	110	0.09	1.08	0.333	0.5120255	1	10065
GTPASE_ACTIVITY	97	0.1	1.08	0.347	0.5116993	1	7229
ORGANELLE_OUTER_MEMBRANE	23	0.19	1.08	0.367	0.5197569	1	2882
REGULATION_OF_ORGANELLE_ORGANIZATIO	38	0.15	1.08	0.362	0.5192235	1	5938
GLYCOPROTEIN_METABOLIC_PROCESS	90	0.1	1.07	0.371	0.5208495	1	9929
VESICULAR_FRACTION	44	0.13	1.06	0.358	0.5342453	1	3330
PIGMENT_METABOLIC_PROCESS	18	0.21	1.05	0.375	0.5477152	1	7250
DOUBLE_STRANDED_DNA_BINDING	32	0.16	1.05	0.383	0.5515322	1	3351
ELECTRON_TRANSPORT_GO_0006118	51	0.13	1.04	0.389	0.5708567	1	6243
SMALL_GTPASE_MEDIATED_SIGNAL_TRANSD	86	0.1	1.03	0.421	0.5803943	1	9838
ANION_CHANNEL_ACTIVITY	20	0.19	1.03	0.391	0.5817772	1	8262
NUCLEAR_HORMONE_RECEPTOR_BINDING	28	0.17	1.03	0.401	0.5837079	1	13755
CARBON_OXYGEN_LYASE_ACTIVITY	31	0.15	1.02	0.423	0.5912336	1	10659
TRANSFERASE_ACTIVITY_TRANSFERRING_PEP	20	0.19	1.02	0.421	0.5916135	1	11903
PROTEIN_DOMAIN_SPECIFIC_BINDING	70	0.1	1.02	0.396	0.5936737	1	7435
MOTOR_ACTIVITY	27	0.16	1.02	0.403	0.5932146	1	4398
REGULATION_OF_G_PROTEIN_COUPLED_REC	22	0.18	1.02	0.405	0.5935388	1	10699
CYTOPLASMIC_VESICLE_MEMBRANE	26	0.16	1.02	0.403	0.5957698	1	1196
DI___TRI_VALENT_INORGANIC_CATION_TRA	22	0.18	1.01	0.421	0.5955539	1	14821
CELL_MATRIX_ADHESION	37	0.14	1.01	0.445	0.59645	1	9143
OUTER_MEMBRANE	24	0.17	1.01	0.41	0.5953157	1	2882
PROTEIN_DIMERIZATION_ACTIVITY	178	0.07	1.01	0.419	0.5988138	1	14865
PRIMARY_ACTIVE_TRANSMEMBRANE_TRANS	40	0.13	1.01	0.42	0.6038892	1	13439
INORGANIC_ANION_TRANSMEMBRANE_TRA	19	0.19	1	0.428	0.6044837	1	12816
PHOSPHORIC_DIESTER_HYDROLASE_ACTIVITY	40	0.13	1	0.462	0.6127294	1	14796
CYTOPLASMIC_VESICLE_PART	26	0.16	1	0.437	0.6129253	1	1196
RESPONSE_TO_RADIATION	56	0.11	0.99	0.448	0.619849	1	10846
REGULATION_OF_CELL_GROWTH	43	0.13	0.99	0.443	0.6195851	1	10320
ATPASE_ACTIVITY_COUPLED_TO_MOVEMENT	40	0.13	0.99	0.417	0.6206257	1	13439
CYSTEINE_TYPE_ENDOPEPTIDASE_ACTIVITY	40	0.13	0.99	0.465	0.6237305	1	8940

STRUCTURAL_CONSTITUENT_OF_CYTOSKELET	56	0.11	0.99	0.447	0.6242542	1	7634
LIPID_BIOSYNTHETIC_PROCESS	96	0.09	0.99	0.474	0.6237072	1	5034
CELL_STRUCTURE_DISASSEMBLY_DURING_AI	17	0.2	0.98	0.465	0.6243214	1	8054
GTPASE_BINDING	34	0.14	0.98	0.445	0.6263732	1	10199
POSITIVE_REGULATION_OF_CELLULAR_PROT	72	0.1	0.98	0.456	0.6303877	1	8996
POSITIVE_REGULATION_OF_BINDING	26	0.16	0.98	0.456	0.6287155	1	4114
MICROSOME	42	0.13	0.98	0.495	0.6308575	1	3330
DEPHOSPHORYLATION	68	0.1	0.97	0.482	0.640869	1	12545
POSITIVE_REGULATION_OF_CELL_PROLIFERA	147	0.07	0.97	0.453	0.6418493	1	8133
RHO_GTPASE_ACTIVATOR_ACTIVITY	19	0.19	0.97	0.49	0.6445515	1	13766
PROTEIN_AUTOPROCESSING	31	0.15	0.96	0.489	0.6478772	1	10204
HYDROLASE_ACTIVITY_ACTING_ON_ACID_AN	39	0.13	0.96	0.495	0.6507243	1	13439
PHOSPHORIC_MONOESTER_HYDROLASE_ACT	108	0.08	0.96	0.479	0.6502913	1	12153
VIRAL_GENOME_REPLICATION	21	0.17	0.96	0.499	0.6488931	1	2017
DEFENSE_RESPONSE_TO_BACTERIUM	24	0.16	0.95	0.496	0.6571185	1	13611
EXTRACELLULAR_LIGAND_GATED_ION_CHAN	22	0.17	0.95	0.522	0.6622171	1	12560
APICAL_PART_OF_CELL	16	0.2	0.95	0.507	0.6655374	1	9896
REGULATION_OF_BLOOD_PRESSURE	22	0.17	0.94	0.511	0.6674599	1	11731
HYDRO_LYASE_ACTIVITY	27	0.15	0.94	0.513	0.6668181	1	10659
ATPASE_ACTIVITY_COUPLED_TO_TRANSMEN	20	0.17	0.94	0.513	0.666437	1	14056
OXIDOREDUCTASE_ACTIVITY_ACTING_ON_TH	22	0.17	0.94	0.513	0.6726957	1	7663
CARBOHYDRATE_TRANSPORT	18	0.18	0.94	0.509	0.6739717	1	10757
RESPONSE_TO_LIGHT_STIMULUS	43	0.12	0.93	0.537	0.6769325	1	7960
SH3_DOMAIN_BINDING	15	0.2	0.93	0.528	0.6777821	1	9667
VESICLE_MEMBRANE	28	0.15	0.93	0.52	0.6769146	1	1196
CYTOSKELETAL_PROTEIN_BINDING	156	0.06	0.93	0.532	0.6848877	1	10018
SMALL_GTPASE_BINDING	33	0.13	0.92	0.549	0.6849805	1	12905
G1_PHASE	15	0.2	0.92	0.561	0.6907011	1	7323
RAS_GTPASE_BINDING	25	0.15	0.92	0.546	0.6955432	1	15296
EXCRETION	36	0.13	0.92	0.559	0.6950568	1	13231
LAMELLIPODIUM	25	0.16	0.91	0.561	0.6951398	1	9451
HYDROLASE_ACTIVITY_ACTING_ON_CARBON	21	0.17	0.91	0.521	0.7010029	1	9052
GLYCOLIPID_METABOLIC_PROCESS	16	0.19	0.91	0.551	0.6994799	1	8996
CARBOHYDRATE_METABOLIC_PROCESS	177	0.06	0.91	0.582	0.7008496	1	9336
POSITIVE_REGULATION_OF_CELL_DIFFERENT	25	0.15	0.91	0.57	0.7028377	1	3759
RHO_PROTEIN_SIGNAL_TRANSDUCTION	38	0.12	0.91	0.58	0.7019655	1	9667
REGULATION_OF_SMALL_GTPASE_MEDIATEI	23	0.16	0.9	0.59	0.7035962	1	9667
TRANSITION_METAL_ION_BINDING	107	0.08	0.9	0.567	0.7048617	1	1354
NEURON_APOPTOSIS	17	0.18	0.9	0.563	0.7036156	1	8435
EXCITATORY_EXTRACELLULAR_LIGAND_GATE	21	0.16	0.9	0.548	0.7067341	1	12560
T_CELL_ACTIVATION	42	0.12	0.89	0.566	0.7178453	1	12123
ICOSANOID_METABOLIC_PROCESS	16	0.19	0.89	0.561	0.7178978	1	10158
LIPOPROTEIN_METABOLIC_PROCESS	32	0.13	0.89	0.543	0.7173172	1	4958
MICROTUBULE_MOTOR_ACTIVITY	15	0.19	0.89	0.608	0.7164925	1	14704
CELLULAR_CARBOHYDRATE_METABOLIC_PR(	124	0.07	0.89	0.596	0.7152607	1	5477
AROMATIC_COMPOUND_METABOLIC_PROCI	26	0.14	0.89	0.612	0.7158351	1	14783
OXYGEN_AND_REACTIVE_OXYGEN_SPECIES_	20	0.16	0.89	0.608	0.7170757	1	1559
NUCLEAR_ORGANIZATION_AND_BIOGENESIS	29	0.14	0.88	0.573	0.7179056	1	6858
GLYCEROPHOSPHOLIPID_BIOSYNTHETIC_PRC	29	0.14	0.88	0.6	0.7182066	1	4958
PROTEIN_AMINO_ACID_DEPHOSPHORYLATIC	61	0.09	0.88	0.616	0.7213091	1	13120
CARBOHYDRATE_TRANSMEMBRANE_TRANSF	15	0.19	0.87	0.613	0.7361823	1	11104
DENDRITE	16	0.18	0.87	0.629	0.7359166	1	9104
EXTERNAL_SIDE_OF_PLASMA_MEMBRANE	15	0.18	0.86	0.624	0.7522797	1	14781
CELL_CORTEX_PART	23	0.15	0.85	0.648	0.762871	1	6768
APOPTOTIC_PROGRAM	58	0.1	0.85	0.635	0.76125	1	6074
CALMODULIN_BINDING	25	0.14	0.85	0.659	0.7662347	1	14118
ZINC_ION_BINDING	86	0.08	0.84	0.667	0.7728202	1	1558
ATP_BINDING	149	0.06	0.84	0.652	0.7784304	1	16167
SECONDARY_METABOLIC_PROCESS	26	0.14	0.84	0.672	0.777356	1	7250
GLYCOSAMINOGLYCAN_BINDING	34	0.12	0.83	0.61	0.7830359	1	8468
PHOSPHOLIPASE_C_ACTIVITY	15	0.17	0.83	0.692	0.7868146	1	13730
ADENYL_NUCLEOTIDE_BINDING	162	0.06	0.83	0.673	0.789273	1	16167
SECRETION	175	0.05	0.82	0.669	0.7936855	1	14124
DETECTION_OF_EXTERNAL_STIMULUS	21	0.15	0.82	0.707	0.7951261	1	11928
DRUG_BINDING	16	0.17	0.82	0.683	0.8023614	1	4854
ACTIN_CYTOSKELETON	127	0.06	0.81	0.695	0.8050538	1	7126
ONE_CARBON_COMPOUND_METABOLIC_PR	26	0.13	0.81	0.699	0.8068487	1	5956
EMBRYONIC_DEVELOPMENT	56	0.09	0.81	0.691	0.8099189	1	4479
REGULATION_OF_RAS_PROTEIN_SIGNAL_TR/	19	0.15	0.8	0.706	0.8198425	1	9667
COENZYME_BINDING	16	0.17	0.8	0.708	0.822352	1	11702
PURINE_RIBONUCLEOTIDE_BINDING	195	0.05	0.79	0.729	0.8249762	1	3674

DOUBLE_STRANDED_RNA_BINDING	17	0.16	0.79	0.74	0.8257941	1	5617
ADENYL_RIBONUCLEOTIDE_BINDING	156	0.05	0.79	0.754	0.8267236	1	16167
ANION_TRANSMEMBRANE_TRANSPORTER_A	59	0.09	0.78	0.724	0.8352163	1	12816
PROTEIN_KINASE_BINDING	60	0.08	0.77	0.766	0.8542843	1	11445
CLATHRIN_COATED_VESICLE	35	0.11	0.76	0.78	0.8632302	1	8368
RESPONSE_TO_OXIDATIVE_STRESS	44	0.1	0.76	0.768	0.8651534	1	9339
FEMALE_GAMETE_GENERATION	16	0.16	0.76	0.782	0.8667259	1	15248
SIGNAL_SEQUENCE_BINDING	15	0.16	0.76	0.777	0.8666504	1	12689
HETEROCYCLE_METABOLIC_PROCESS	26	0.12	0.75	0.794	0.8690425	1	4749
POSITIVE_REGULATION_OF_CYTOKINE_PROD	15	0.16	0.75	0.776	0.8688683	1	7960
TRANSCRIPTION_COREPRESSOR_ACTIVITY	89	0.07	0.75	0.786	0.8680415	1	1430
L_AMINO_ACID_TRANSMEMBRANE_TRANSP	16	0.15	0.75	0.782	0.8755097	1	5146
REGULATION_OF_GENE_EXPRESSION_EPIGEN	30	0.12	0.74	0.783	0.8754586	1	6338
GTPASE_ACTIVATOR_ACTIVITY	58	0.08	0.74	0.782	0.8742883	1	13766
SULFUR_METABOLIC_PROCESS	37	0.1	0.74	0.81	0.8727968	1	8952
CELL_SUBSTRATE_ADHERENS_JUNCTION	15	0.16	0.74	0.802	0.8773028	1	15242
REGULATION_OF_MITOTIC_CELL_CYCLE	23	0.12	0.73	0.804	0.8870936	1	10320
PROTEIN_SECRETION	32	0.11	0.72	0.825	0.9026672	1	4859
CELLULAR_RESPONSE_TO_STIMULUS	18	0.14	0.72	0.804	0.9010868	1	4537
MICROTUBULE_BASED_MOVEMENT	15	0.15	0.72	0.835	0.9010982	1	3292
REGULATION_OF_GROWTH	55	0.08	0.71	0.818	0.9088881	1	10340
NEGATIVE_REGULATION_OF_CELL_MIGRATIC	15	0.15	0.7	0.845	0.9146273	1	11741
CYSTEINE_TYPE_PEPTIDASE_ACTIVITY	54	0.08	0.69	0.859	0.9244298	1	16302
CHROMATIN_REMODELING_COMPLEX	17	0.14	0.69	0.879	0.9243422	1	2848
INTERMEDIATE_FILAMENT_CYTOSKELETON	23	0.12	0.68	0.851	0.9299429	1	7293
NEGATIVE_REGULATION_OF_TRANSPORT	20	0.13	0.68	0.853	0.9325887	1	6673
INTERMEDIATE_FILAMENT	23	0.12	0.67	0.871	0.9409125	1	7293
CELL_PROJECTION_BIOGENESIS	24	0.11	0.67	0.871	0.9394405	1	10751
PROTEIN_BINDING_BRIDGING	57	0.07	0.67	0.868	0.9380548	1	7243
INTRACELLULAR_RECEPTOR_MEDIATED_SIGN	21	0.12	0.67	0.886	0.936689	1	14193
ANTIOXIDANT_ACTIVITY	17	0.14	0.66	0.888	0.9449276	1	15623
RAS_GTPASE_ACTIVATOR_ACTIVITY	29	0.1	0.66	0.906	0.9488927	1	13766
HOMEOSTASIS_OF_NUMBER_OF_CELLS	20	0.12	0.65	0.877	0.9478623	1	3189
CELLULAR_CARBOHYDRATE_CATABOLIC_PRC	21	0.12	0.65	0.891	0.9474584	1	13318
NEGATIVE_REGULATION_OF_MAP_KINASE_A	17	0.13	0.65	0.879	0.9462143	1	2990
LYSOSOME	61	0.07	0.65	0.89	0.9466921	1	15936
PEPTIDYL_TYROSINE_PHOSPHORYLATION	27	0.11	0.65	0.9	0.948657	1	8816
ER_NUCLEAR_SIGNALING_PATHWAY	15	0.14	0.65	0.904	0.9466912	1	14370
LYTIC_VACUOLE	61	0.07	0.63	0.921	0.9556261	1	15936
DNA_PACKAGING	35	0.09	0.62	0.906	0.9627561	1	1498
REGULATION_OF_PROTEIN_SECRETION	22	0.11	0.62	0.926	0.9651393	1	4565
STEROID_HORMONE_RECEPTOR_SIGNALING_	20	0.12	0.61	0.923	0.9677289	1	14193
REGULATION_OF_ENDOCYTOSIS	16	0.13	0.61	0.915	0.9666479	1	15758
POSITIVE_REGULATION_OF_CELL_CYCLE	15	0.13	0.61	0.928	0.9675875	1	15720
CYTOSKELETON_DEPENDENT_INTRACELLULA	25	0.1	0.6	0.941	0.974062	1	3292
OXIDOREDUCTASE_ACTIVITY_ACTING_ON_NA	25	0.1	0.59	0.949	0.974438	1	4728
SPHINGOLIPID_METABOLIC_PROCESS	29	0.09	0.58	0.961	0.9850537	1	8996
CARBOHYDRATE_BIOSYNTHETIC_PROCESS	49	0.07	0.57	0.956	0.985245	1	6499
CARBON_CARBON_LYASE_ACTIVITY	18	0.11	0.56	0.96	0.988933	1	11082
EMBRYONIC_MORPHOGENESIS	17	0.11	0.55	0.966	0.9906001	1	3310
INTEGRAL_TO_ENDOPLASMIC_RETICULUM_N	23	0.09	0.55	0.968	0.9901254	1	6951
NEGATIVE_REGULATION_OF_CELL_ADHESIOI	17	0.11	0.54	0.982	0.9921145	1	10779
INTRINSIC_TO_ENDOPLASMIC_RETICULUM_N	23	0.09	0.54	0.977	0.9923444	1	6951
MAINTENANCE_OF_LOCALIZATION	22	0.09	0.52	0.99	0.9950578	1	16411
PHOSPHOPROTEIN_PHOSPHATASE_ACTIVITY	79	0.05	0.52	0.988	0.9944938	1	12153
OXIDOREDUCTASE_ACTIVITY_ACTING_ON_CI	61	0.05	0.5	0.984	0.9981275	1	9095
COPPER_ION_BINDING	15	0.1	0.48	0.998	0.9987205	1	11397
OXIDOREDUCTASE_ACTIVITY_GO_0016616	55	0.05	0.46	0.998	1	1	13540
CELL_PROJECTION_PART	19	0.09	0.45	0.996	0.9985749	1	6052
ENDOSOME	67	0.04	0.44	1	0.9977413	1	5936

Table S3 | Gene Set Enrichment Analysis output for negative selection of essential genes in HUES62 hES cells after 14 additional days in culture. For the analysis, the *ALL Gene Ontology* set was used from the Moleular Signatures Database (MSigDB) with a minimum set size of 50 and max set size of 200.

NAME	SIZE	ES	NES	NOMp	FDRq	FWERp	RANK AT MAX
STRUCTURAL_CONSTITUENT_OF_RIBOSOME	76	0.3	3.2	0	0	0	3859
CHROMOSOMAL_PART	94	0.3	3.1	0	0	0	6631
TRANSLATION	171	0.2	3.1	0	0	0	6618
KINETOCHORE	24	0.5	2.9	0	9.40E-04	0.003	3761
RNA_PROCESSING	169	0.2	2.9	0	7.52E-04	0.003	5236
RNA_SPLICING	90	0.3	2.9	0	6.27E-04	0.003	4320
RNA_POLYMERASE_ACTIVITY	15	0.6	2.8	0	7.19E-04	0.004	2256
CHROMOSOME	120	0.2	2.8	0	0.00141	0.009	5702
RIBONUCLEOPROTEIN_COMPLEX	141	0.2	2.7	0	0.00208	0.015	4002
ENDONUCLEASE_ACTIVITY	25	0.4	2.6	0	0.00459	0.037	8117
CHROMOSOMEPERICENTRIC_REGION	30	0.4	2.6	0	0.00584	0.052	3761
SMALL_NUCLEAR_RIBONUCLEOPROTEIN_C	22	0.4	2.5	0	0.01266	0.117	3794
MRNA_METABOLIC_PROCESS	81	0.2	2.2	0	0.04974	0.403	5155
MRNA_PROCESSING_GO_0006397	71	0.2	2.2	0	0.04785	0.414	4776
RIBONUCLEASE_ACTIVITY	25	0.4	2.2	0	0.04614	0.422	8287
RIBONUCLEOPROTEIN_COMPLEX_BIOGENES	82	0.2	2.2	0	0.04803	0.451	7292
DNA_REPLICATION	99	0.2	2.2	0	0.04989	0.481	6509
DENDRITE	16	0.5	2.2	0	0.04712	0.481	9662
NEGATIVE_REGULATION_OF_DNA_METABO	18	0.4	2.2	0.002	0.05343	0.542	5309
SPINDLE_POLE	18	0.4	2.2	0	0.0537	0.562	7479
UBIQUITIN_CYCLE	48	0.3	2.1	0	0.06029	0.637	6612
BIOPOLYMER_CATABOLIC_PROCESS	113	0.2	2.1	0.002	0.06013	0.651	10475
MICROTUBULE_ORGANIZING_CENTER	65	0.2	2.1	0.002	0.06211	0.684	9572
NUCLEOLUS	121	0.2	2.1	0.002	0.07798	0.778	3586
SPLICEOSOME	50	0.3	2.1	0.004	0.07747	0.789	3794
PROTEIN_CATABOLIC_PROCESS	67	0.2	2.1	0.006	0.08273	0.821	6846
MACROMOLECULE_CATABOLIC_PROCESS	131	0.2	2	0.006	0.08604	0.836	10475
CENTROSOME	56	0.2	2	0.006	0.08482	0.841	9426
RNA_SPLICINGVIA_TRANSESTERIFICATION_R	34	0.3	2	0.004	0.10577	0.915	4320
PATTERN_BINDING	45	0.2	2	0	0.10286	0.917	6020
POSITIVE_REGULATION_OF_PHOSPHORYLAT	26	0.3	1.9	0.002	0.14238	0.967	7503
MICROTUBULE_CYTOSKELETON	148	0.1	1.9	0.008	0.1459	0.97	9916
RESPONSE_TO_HORMONE_STIMULUS	32	0.3	1.9	0.01	0.15685	0.981	7269
REGULATION_OF_PHOSPHORYLATION	48	0.2	1.9	0.008	0.15934	0.985	8616
NEGATIVE_REGULATION_OF_CELLULAR_BIO	29	0.3	1.9	0.019	0.17987	0.993	8483
HEART_DEVELOPMENT	36	0.3	1.9	0.006	0.17584	0.993	8825
NUCLEOLAR_PART	17	0.4	1.9	0.018	0.17614	0.993	8101
DNA_DEPENDENT_DNA_REPLICATION	53	0.2	1.9	0.006	0.17392	0.994	6368
POSITIVE_REGULATION_OF_PROTEIN_AMIN	20	0.3	1.9	0.01	0.17751	0.995	7503
EMBRYONIC_DEVELOPMENT	56	0.2	1.8	0.012	0.18565	0.997	9425
PROTEIN_UBIQUITINATION	40	0.2	1.8	0.011	0.18796	0.997	6042
PHAGOCYTOSIS	16	0.4	1.8	0.004	0.18496	0.997	4338
NUCLEOTIDYLTRANSFERASE_ACTIVITY	46	0.2	1.8	0.021	0.19598	0.997	2256
HORMONE_RECEPTOR_BINDING	29	0.3	1.8	0.01	0.19662	0.998	9791
NUCLEASE_ACTIVITY	55	0.2	1.8	0.012	0.19249	0.998	8287
BASAL_LAMINA	21	0.3	1.8	0.017	0.19215	0.998	6036
CHROMOSOME_SEGREGATION	32	0.3	1.8	0.013	0.2076	0.999	3761
SPINDLE	37	0.3	1.8	0.015	0.20624	0.999	8644
MITOSIS	81	0.2	1.8	0.02	0.20972	1	4967
STRUCTURAL_CONSTITUENT_OF_MUSCLE	32	0.3	1.8	0.013	0.21334	1	11158
DAMAGED_DNA_BINDING	20	0.3	1.8	0.014	0.21846	1	7506
M_PHASE_OF_MITOTIC_CELL_CYCLE	84	0.2	1.8	0.018	0.21511	1	4967
NUCLEAR_HORMONE_RECEPTOR_BINDING	28	0.3	1.8	0.022	0.21215	1	9791
OXIDOREDUCTASE_ACTIVITY_ACTING_ON_T	15	0.4	1.8	0.025	0.21138	1	7735
PROTEIN_MODIFICATION_BY_SMALL_PROTE	43	0.2	1.8	0.03	0.22156	1	6042
GUANYL_NUCLEOTIDE_EXCHANGE_FACTOR_	46	0.2	1.7	0.022	0.21841	1	13024
SMALL_CONJUGATING_PROTEIN_LIGASE_A	51	0.2	1.7	0.021	0.21631	1	5497
REGULATION_OF_MUSCLE_CONTRACTION	19	0.3	1.7	0.022	0.21511	1	11302
POSITIVE_REGULATION_OF_PROTEIN_META	74	0.2	1.7	0.012	0.21577	1	7162
REGULATION_OF_TRANSFERASE_ACTIVITY	155	0.1	1.7	0.04	0.2136	1	11602
TRANSCRIPTION_FROM_RNA_POLYMERASE_	19	0.3	1.7	0.024	0.21834	1	4493
MITOTIC_CELL_CYCLE	152	0.1	1.7	0.035	0.2149	1	4967
PROTEIN_RNA_COMPLEX_ASSEMBLY	63	0.2	1.7	0.03	0.2164	1	7239
RNA_POLYMERASE_COMPLEX	17	0.3	1.7	0.024	0.21365	1	2256
DNA_DIRECTED_RNA_POLYMERASE_COMPL	17	0.3	1.7	0.036	0.21796	1	2256
NEGATIVE_REGULATION_OF_BIOSYNTHETIC_	30	0.3	1.7	0.02	0.2195	1	8483

NUCLEAR_DNA_DIRECTED_RNA_POLYMERA	17	0.3	1.7	0.019	0.21845	1	2256
MITOTIC_SISTER_CHROMATID_SEGREGATIO	16	0.4	1.7	0.028	0.22184	1	3761
GTP_BINDING	43	0.2	1.7	0.025	0.21892	1	3196
REPLICATION_FORK	17	0.3	1.7	0.031	0.22204	1	9948
TRANSLATION_INITIATION_FACTOR_ACTIVIT	22	0.3	1.7	0.026	0.21986	1	9299
DOUBLE_STRAND_BREAK_REPAIR	23	0.3	1.7	0.028	0.21749	1	6462
REGULATION_OF_PROTEIN_KINASE_ACTIVIT	149	0.1	1.7	0.034	0.21502	1	11602
MICROTUBULE_ORGANIZING_CENTER_PART	19	0.3	1.7	0.032	0.21365	1	9335
SMALL_GTPASE_MEDIATED_SIGNAL_TRANS	86	0.2	1.7	0.02	0.21254	1	11491
REGULATION_OF_KINASE_ACTIVITY	151	0.1	1.7	0.025	0.21612	1	11602
UBIQUITIN_PROTEIN_LIGASE_ACTIVITY	49	0.2	1.7	0.024	0.21416	1	5497
SMALL_PROTEIN_CONJUGATING_ENZYME_	52	0.2	1.7	0.025	0.21637	1	5497
GUANYL_NUCLEOTIDE_BINDING	44	0.2	1.7	0.038	0.24144	1	3196
POSITIVE_REGULATION_OF_PHOSPHATE_M	28	0.3	1.7	0.043	0.24026	1	7503
PROTEIN_FOLDING	56	0.2	1.7	0.036	0.24292	1	4076
CARBOHYDRATE_BINDING	70	0.2	1.6	0.035	0.25783	1	6020
MICROTUBULE_CYTOSKELETON_ORGANIZAT	33	0.2	1.6	0.04	0.25856	1	6113
LIPID_TRANSPORT	28	0.3	1.6	0.038	0.25897	1	12141
DNA_INTEGRITY_CHECKPOINT	23	0.3	1.6	0.03	0.25667	1	5166
TRANSLATION_REGULATOR_ACTIVITY	37	0.2	1.6	0.033	0.27763	1	9515
LIGASE_ACTIVITY	94	0.1	1.6	0.047	0.27909	1	5497
HEPARIN_BINDING	23	0.3	1.6	0.043	0.27788	1	5955
REGULATION_OF_PROTEIN_METABOLIC_PR	167	0.1	1.6	0.043	0.27482	1	7269
POSITIVE_REGULATION_OF_CELLULAR_PROT	72	0.2	1.6	0.038	0.27409	1	7162
INTEGRIN_COMPLEX	19	0.3	1.6	0.04	0.27547	1	8862
POLYSACCHARIDE_BINDING	36	0.2	1.6	0.037	0.27799	1	6020
TRANSMISSION_OF_NERVE_IMPULSE	183	0.1	1.6	0.048	0.27746	1	11412
RESPONSE_TO_ENDOGENOUS_STIMULUS	194	0.1	1.6	0.022	0.27466	1	6712
OXIDOREDUCTASE_ACTIVITY_ACTING_ON_T	21	0.3	1.6	0.04	0.28801	1	7735
CONTRACTILE_FIBER_PART	23	0.3	1.6	0.041	0.29314	1	11457
SYNAPTIC_TRANSMISSION	168	0.1	1.6	0.043	0.29093	1	11710
SISTER_CHROMATID_SEGREGATION	17	0.3	1.6	0.065	0.2922	1	3761
GLYCOSAMINOGLYCAN_BINDING	34	0.2	1.6	0.063	0.29084	1	6020
CELLULAR_PROTEIN_CATABOLIC_PROCESS	57	0.2	1.6	0.049	0.28838	1	6327
RAS_GUANYL_NUCLEOTIDE_EXCHANGE_FAC	19	0.3	1.6	0.047	0.29365	1	10881
NEGATIVE_REGULATION_OF_TRANSLATION	23	0.3	1.6	0.056	0.31103	1	6953
ATP_DEPENDENT_HELICASE_ACTIVITY	27	0.2	1.5	0.057	0.32931	1	2855
COPPER_ION_BINDING	15	0.3	1.5	0.067	0.32727	1	9758
CELLULAR_MACROMOLECULE_CATABOLIC_	100	0.1	1.5	0.048	0.32471	1	12464
TRANSLATION_FACTOR_ACTIVITY_NUCLEIC_	35	0.2	1.5	0.059	0.32627	1	9515
POSITIVE_REGULATION_OF_PROTEIN_MODI	29	0.2	1.5	0.065	0.33125	1	7503
SMALL_GTPASE_REGULATOR_ACTIVITY	67	0.2	1.5	0.068	0.33907	1	13591
REGULATION_OF_PROTEIN_AMINO_ACID_P	30	0.2	1.5	0.075	0.34761	1	8455
TRANSCRIPTION_ACTIVATOR_ACTIVITY	172	0.1	1.5	0.045	0.34691	1	9559
M_PHASE	113	0.1	1.5	0.072	0.34708	1	6114
ACID_AMINO_ACID_LIGASE_ACTIVITY	57	0.2	1.5	0.084	0.36944	1	5497
CYTOKINE_PRODUCTION	72	0.2	1.5	0.081	0.36709	1	13356
MICROTUBULE	30	0.2	1.5	0.078	0.37229	1	8552
SEQUENCE_SPECIFIC_DNA_BINDING	57	0.2	1.5	0.059	0.37065	1	11611
REGULATION_OF_CELL_CYCLE	177	0.1	1.5	0.073	0.36903	1	3995
THYROID_HORMONE_RECEPTOR_BINDING	17	0.3	1.5	0.075	0.37066	1	9448
CONTRACTILE_FIBER	25	0.2	1.5	0.065	0.37457	1	11457
PROTEIN_DIMERIZATION_ACTIVITY	178	0.1	1.5	0.075	0.37188	1	10558
REGULATION_OF_DNA_METABOLIC_PROCE	45	0.2	1.5	0.078	0.37703	1	6709
LIGASE_ACTIVITY_FORMING_CARBON_NITR	67	0.2	1.5	0.086	0.39831	1	13750
MEDIATOR_COMPLEX	18	0.3	1.5	0.087	0.3967	1	7899
REGULATED_SECRETORY_PATHWAY	15	0.3	1.5	0.086	0.3938	1	8732
EXTRACELLULAR_LIGAND_GATED_ION_CHA	22	0.3	1.5	0.088	0.39176	1	11688
INORGANIC_ANION_TRANSPORT	18	0.3	1.5	0.081	0.39574	1	10957
RRNA_METABOLIC_PROCESS	16	0.3	1.4	0.089	0.40759	1	8117
REGULATION_OF_ANGIOGENESIS	26	0.2	1.4	0.086	0.4061	1	10381
DEOXYRIBONUCLEASE_ACTIVITY	22	0.3	1.4	0.11	0.41665	1	10991
DNA_DIRECTED_RNA_POLYMERASEII_HOLO	66	0.1	1.4	0.082	0.42062	1	2256
CONDENSED_CHROMOSOME	33	0.2	1.4	0.084	0.4268	1	6080
SPLICEOSOME_ASSEMBLY	21	0.3	1.4	0.102	0.4237	1	3073
REGULATION_OF_TRANSLATION	90	0.1	1.4	0.075	0.42146	1	6953
NUCLEAR_CHROMOSOME_PART	33	0.2	1.4	0.108	0.42265	1	6085
EXCITATORY_EXTRACELLULAR_LIGAND_GAT	21	0.3	1.4	0.102	0.41963	1	11688
RESPONSE_TO_UV	25	0.2	1.4	0.112	0.41962	1	6509
CELL_CYCLE_PHASE	169	0.1	1.4	0.075	0.41901	1	6114
INTERACTION_WITH_HOST	17	0.3	1.4	0.101	0.41987	1	9746

MITOCHONDRIAL_PART	138	0.1	1.4	0.099	0.41691	1	10078
LIPID_HOMEOSTASIS	15	0.3	1.4	0.112	0.42099	1	11357
GROWTH_FACTOR_ACTIVITY	52	0.2	1.4	0.103	0.41814	1	9943
PROTEIN_C_TERMINUS_BINDING	70	0.1	1.4	0.089	0.42263	1	11598
ACTIN_FILAMENT_BASED_PROCESS	113	0.1	1.4	0.094	0.42559	1	9015
OXYGEN_AND_REACTIVE_OXYGEN_SPECIES_	20	0.3	1.4	0.12	0.42292	1	9758
STEROID_HORMONE_RECEPTOR_SIGNALING	20	0.3	1.4	0.11	0.42807	1	3365
ORGANELLE_INNER_MEMBRANE	72	0.1	1.4	0.106	0.45011	1	10063
ORGANELLE_LOCALIZATION	24	0.2	1.4	0.124	0.44814	1	6325
APOPTOTIC_PROGRAM	58	0.2	1.4	0.113	0.44969	1	10241
PROTEIN_HOMODIMERIZATION_ACTIVITY	118	0.1	1.4	0.12	0.45711	1	11861
TRANSCRIPTION_REPRESSOR_ACTIVITY	147	0.1	1.4	0.12	0.46068	1	7709
CENTRAL_NERVOUS_SYSTEM_DEVELOPMEN	121	0.1	1.4	0.117	0.45862	1	10198
EXCRETION	36	0.2	1.4	0.113	0.47181	1	13091
POSITIVE_REGULATION_OF_CELLULAR_COM	34	0.2	1.4	0.132	0.4797	1	10253
TRANSCRIPTION_COREPRESSOR_ACTIVITY	89	0.1	1.4	0.119	0.48185	1	7709
CELL_SUBSTRATE_ADHESION	38	0.2	1.4	0.118	0.48259	1	10434
ACTIN_CYTOSKELETON_ORGANIZATION_AN	103	0.1	1.4	0.156	0.48095	1	9015
REGULATION_OF_CELLULAR_PROTEIN_MET	157	0.1	1.3	0.114	0.48962	1	7269
MAINTENANCE_OF_LOCALIZATION	22	0.2	1.3	0.14	0.49435	1	10410
SUGAR_BINDING	32	0.2	1.3	0.141	0.49252	1	4815
RESPONSE_TO_ORGANIC_SUBSTANCE	29	0.2	1.3	0.139	0.49164	1	11861
RESPONSE_TO_BACTERIUM	29	0.2	1.3	0.143	0.49544	1	9231
CELL_MATURATION	16	0.3	1.3	0.13	0.49614	1	6257
INTRACELLULAR_RECEPTOR_MEDIATED_SIG	21	0.2	1.3	0.155	0.49335	1	3365
CHROMATIN	35	0.2	1.3	0.16	0.49924	1	6463
ISOMERASE_ACTIVITY	35	0.2	1.3	0.151	0.5049	1	11648
MOTOR_ACTIVITY	27	0.2	1.3	0.136	0.51497	1	9498
RAS_PROTEIN_SIGNAL_TRANSDUCTION	65	0.1	1.3	0.139	0.5177	1	11457
GTPASE_REGULATOR_ACTIVITY	123	0.1	1.3	0.156	0.51778	1	10421
REGULATION_OF_DNA_REPLICATION	20	0.2	1.3	0.155	0.52449	1	6368
VITAMIN_METABOLIC_PROCESS	17	0.3	1.3	0.163	0.53823	1	6955
CELL_MATRIX_ADHESION	37	0.2	1.3	0.149	0.54069	1	10434
RRNA_PROCESSING	15	0.3	1.3	0.189	0.54188	1	4442
RIBOSOME	39	0.2	1.3	0.151	0.53915	1	3769
REGULATION_OF_CYTOKINE_PRODUCTION	24	0.2	1.3	0.167	0.5363	1	13356
INTRAMOLECULAR_OXIDOREDUCTASE_ACTI	19	0.3	1.3	0.171	0.53496	1	11648
TRANSMEMBRANE_RECEPTOR_PROTEIN_TY	42	0.2	1.3	0.151	0.53692	1	9016
MICROTUBULE_MOTOR_ACTIVITY	15	0.3	1.3	0.169	0.53437	1	9438
LYMPHOCYTE_ACTIVATION	59	0.1	1.3	0.159	0.53606	1	13078
TRANSCRIPTION_COACTIVATOR_ACTIVITY	122	0.1	1.3	0.15	0.53985	1	9791
REGULATION_OF_BLOOD_PRESSURE	22	0.2	1.3	0.166	0.54833	1	8163
REGULATION_OF_HYDROLASE_ACTIVITY	78	0.1	1.3	0.167	0.54615	1	13329
EMBRYONIC_MORPHOGENESIS	17	0.3	1.3	0.195	0.54896	1	9174
PHOSPHOINOSITIDE_BINDING	19	0.2	1.3	0.178	0.54714	1	12743
DNA_REPAIR	122	0.1	1.3	0.17	0.54761	1	6654
HELICASE_ACTIVITY	50	0.2	1.3	0.178	0.54581	1	7005
LIPID_RAFT	27	0.2	1.3	0.176	0.54598	1	11027
NEGATIVE_REGULATION_OF_TRANSFERASE_	35	0.2	1.3	0.193	0.54404	1	10661
RNA_HELICASE_ACTIVITY	24	0.2	1.3	0.181	0.54428	1	2855
ANION_TRANSPORT	31	0.2	1.3	0.183	0.54349	1	11166
CYTOPLASMIC_VESICLE	114	0.1	1.3	0.179	0.54119	1	10038
NUCLEAR_CHROMOSOME	52	0.1	1.3	0.17	0.54536	1	6085
REGULATION_OF_ACTION_POTENTIAL	17	0.3	1.3	0.176	0.56191	1	1754
ANATOMICAL_STRUCTURE_FORMATION	55	0.1	1.3	0.186	0.56051	1	10542
CELL_CYCLE_PROCESS	191	0.1	1.3	0.186	0.56693	1	6014
TRANSITION_METAL_ION_BINDING	107	0.1	1.3	0.191	0.56557	1	13690
PROTEIN_TYROSINE_KINASE_ACTIVITY	62	0.1	1.3	0.18	0.56271	1	9543
REGULATION_OF_CYTOKINE_BIOSYNTHETIC_	38	0.2	1.3	0.198	0.5627	1	6893
ATPASE_ACTIVITY_COUPLED	93	0.1	1.2	0.18	0.56397	1	9451
ESTABLISHMENT_OF_ORGANELLE_LOCALIZA	18	0.2	1.2	0.189	0.56168	1	2669
RESPONSE_TO_DNA_DAMAGE_STIMULUS	158	0.1	1.2	0.179	0.55953	1	6712
PROTEIN_IMPORT	62	0.1	1.2	0.205	0.56057	1	13349
ENZYME_BINDING	174	0.1	1.2	0.201	0.55886	1	13081
MITOCHONDRIAL_INNER_MEMBRANE	64	0.1	1.2	0.186	0.56755	1	10063
NUCLEAR_ENVELOPE	72	0.1	1.2	0.199	0.56755	1	4008
LIPID_TRANSPORTER_ACTIVITY	28	0.2	1.2	0.208	0.56483	1	10650
REGULATION_OF_CELLULAR_COMPONENT_	118	0.1	1.2	0.199	0.56739	1	10654
ATP_DEPENDENT_RNA_HELICASE_ACTIVITY	17	0.3	1.2	0.23	0.57018	1	2855
ZINC_ION_BINDING	86	0.1	1.2	0.193	0.56991	1	11821
PROTEOGLYCAN_METABOLIC_PROCESS	21	0.2	1.2	0.19	0.56927	1	3735

RESPONSE_TO_TEMPERATURE_STIMULUS	15	0.3	1.2	0.197	0.56757	1	3602
PROTEIN_PROCESSING	48	0.2	1.2	0.189	0.56552	1	10472
REGULATION_OF_MAP_KINASE_ACTIVITY	62	0.1	1.2	0.192	0.56695	1	10421
ENDOSOME_TRANSPORT	23	0.2	1.2	0.217	0.57509	1	12627
PROTEIN_AMINO_ACID_N_LINKED_GLYCOS	30	0.2	1.2	0.221	0.57686	1	5633
MITOCHONDRIAL_MEMBRANE_PART	50	0.1	1.2	0.217	0.57692	1	10063
MICROTUBULE_ORGANIZING_CENTER_ORG	15	0.3	1.2	0.221	0.5756	1	7479
REGULATION_OF_CATABOLIC_PROCESS	16	0.3	1.2	0.218	0.57311	1	12392
COATED_VESICLE_MEMBRANE	15	0.3	1.2	0.229	0.57254	1	10969
SINGLE_STRANDED_DNA_BINDING	33	0.2	1.2	0.221	0.57211	1	5562
CYTOPLASMIC_MEMBRANE_BOUND_VESICL	110	0.1	1.2	0.228	0.57529	1	10038
CELL_CYCLE_CHECKPOINT_GO_0000075	47	0.1	1.2	0.222	0.5844	1	3464
VIRAL_REPRODUCTIVE_PROCESS	36	0.2	1.2	0.234	0.58369	1	9979
CALCIUM_ION_BINDING	101	0.1	1.2	0.232	0.58318	1	13335
DNA_DAMAGE_CHECKPOINT	19	0.2	1.2	0.22	0.58095	1	3464
VIRAL_INFECTIOUS_CYCLE	32	0.2	1.2	0.229	0.58049	1	11514
NEURON_APOPTOSIS	17	0.2	1.2	0.228	0.58144	1	9489
PROTEIN_N_TERMINUS_BINDING	37	0.2	1.2	0.237	0.5828	1	7789
REGULATION_OF_PROTEIN_MODIFICATION_	44	0.2	1.2	0.24	0.58946	1	7503
CARBOHYDRATE_CATABOLIC_PROCESS	22	0.2	1.2	0.226	0.59103	1	13394
MRNA_BINDING	22	0.2	1.2	0.255	0.6017	1	11793
MITOCHONDRIAL_MEMBRANE	82	0.1	1.2	0.254	0.60163	1	10063
RNA_DEPENDENT_ATPASE_ACTIVITY	18	0.2	1.2	0.265	0.59908	1	2855
RNA_POLYMERASE_II_TRANSCRIPTION_FAC	181	0.1	1.2	0.255	0.61099	1	4714
COFACTOR_BINDING	22	0.2	1.2	0.262	0.60896	1	12648
CELLULAR_RESPONSE_TO_STIMULUS	18	0.2	1.2	0.247	0.61	1	4897
GTPASE_BINDING	34	0.2	1.2	0.274	0.60986	1	13432
INOSITOL_OR_PHOSPHATIDYLINOSITOL_KIN	18	0.2	1.2	0.237	0.61108	1	8911
SECRETION	175	0.1	1.2	0.248	0.60985	1	11766
FEEDING_BEHAVIOR	24	0.2	1.2	0.287	0.61331	1	13026
CELLULAR_CARBOHYDRATE_CATABOLIC_PR	21	0.2	1.2	0.262	0.61197	1	13394
TRANSCRIPTION_INITIATION	35	0.2	1.2	0.256	0.62134	1	4203
NEGATIVE_REGULATION_OF_CATALYTIC_AC	69	0.1	1.2	0.249	0.61908	1	10661
ORGANELLE_ENVELOPE	164	0.1	1.2	0.257	0.61992	1	10078
ACETYLCHOLINE_BINDING	17	0.2	1.2	0.266	0.61762	1	10613
ACTIN_BINDING	76	0.1	1.2	0.271	0.61652	1	9547
EXTRINSIC_TO_MEMBRANE	24	0.2	1.2	0.263	0.61628	1	10795
MITOCHONDRION_ORGANIZATION_AND_BI	46	0.1	1.2	0.267	0.61634	1	10720
PROTEIN_AUTOPROCESSING	31	0.2	1.2	0.256	0.61515	1	10242
DEFENSE_RESPONSE_TO_BACTERIUM	24	0.2	1.2	0.261	0.61597	1	9231
DNA_CATABOLIC_PROCESS	22	0.2	1.2	0.258	0.61696	1	10241
RNA_SPLICING_FACTOR_ACTIVITYTRANSEST	19	0.2	1.2	0.279	0.61611	1	3630
REGULATION_OF_GTPASE_ACTIVITY	15	0.2	1.2	0.258	0.61533	1	11305
RECEPTOR_COMPLEX	55	0.1	1.2	0.262	0.62206	1	11772
CHROMOSOME_ORGANIZATION_AND_BIOG	124	0.1	1.1	0.283	0.62595	1	8322
NEGATIVE_REGULATION_OF_CELL_PROLIFE	153	0.1	1.1	0.258	0.62375	1	8852
ATPASE_ACTIVITY	112	0.1	1.1	0.264	0.62767	1	9288
COATED_MEMBRANE	15	0.2	1.1	0.268	0.63037	1	10007
ENVELOPE	164	0.1	1.1	0.262	0.62853	1	10078
MICROTUBULE_BASED_PROCESS	79	0.1	1.1	0.27	0.62648	1	10166
PROTEIN_IMPORT_INTO_NUCLEUS	48	0.1	1.1	0.252	0.62535	1	13349
AMINE_BINDING	23	0.2	1.1	0.291	0.63409	1	10613
RIBOSOME_BIOGENESIS_AND_ASSEMBLY	17	0.2	1.1	0.282	0.6332	1	3361
MITOCHONDRIAL_LUMEN	46	0.1	1.1	0.279	0.63323	1	10077
NUCLEAR_IMPORT	49	0.1	1.1	0.29	0.63405	1	13349
CYTOPLASM_ORGANIZATION_AND_BIOGEN	15	0.2	1.1	0.306	0.63296	1	11290
SMALL_GTPASE_BINDING	33	0.2	1.1	0.298	0.63466	1	13432
MITOCHONDRIAL_MATRIX	46	0.1	1.1	0.292	0.64541	1	10077
ANGIOGENESIS	47	0.1	1.1	0.306	0.64405	1	10542
MICROTUBULE_BINDING	31	0.2	1.1	0.301	0.65093	1	13850
RESPONSE_TO_DRUG	20	0.2	1.1	0.313	0.65551	1	8890
MEMBRANE_COAT	15	0.2	1.1	0.308	0.66618	1	10007
TUBULIN_BINDING	45	0.1	1.1	0.288	0.66384	1	13965
SPHINGOLIPID_METABOLIC_PROCESS	29	0.2	1.1	0.308	0.6616	1	4872
CELL_ACTIVATION	74	0.1	1.1	0.314	0.66419	1	13186
REGULATION_OF_CYCLIN_DEPENDENT_PRO	42	0.1	1.1	0.295	0.6642	1	11593
VIRAL_REPRODUCTION	41	0.1	1.1	0.325	0.6666	1	12362
KINASE_BINDING	68	0.1	1.1	0.317	0.66587	1	7270
TRANSLATIONAL_INITIATION	36	0.2	1.1	0.315	0.66583	1	6263
POSITIVE_REGULATION_OF_NUCLEOBASENU	154	0.1	1.1	0.321	0.66438	1	6743
NEGATIVE_REGULATION_OF_DEVELOPMENT	196	0.1	1.1	0.338	0.66558	1	10974

MYOSIN_COMPLEX	16	0.2	1.1	0.307	0.66468	1	1552
POSITIVE_REGULATION_OF_CELL_CYCLE	15	0.2	1.1	0.326	0.66924	1	4220
CYTOKINE_METABOLIC_PROCESS	42	0.1	1.1	0.334	0.6679	1	6893
REGULATION_OF_SMALL_GTPASE_MEDIATE	23	0.2	1.1	0.325	0.67422	1	11457
PROTEIN_AMINO_ACID_AUTOPHOSPHORYL	30	0.2	1.1	0.335	0.67479	1	10242
RESPONSE_TO_OTHER_ORGANISM	79	0.1	1.1	0.346	0.67616	1	11656
VESICLE_MEDIATED_TRANSPORT	189	0.1	1.1	0.33	0.6756	1	11757
PROTEIN_KINASE_REGULATOR_ACTIVITY	37	0.2	1.1	0.333	0.67858	1	10940
HUMORAL_IMMUNE_RESPONSE	31	0.2	1.1	0.339	0.67909	1	8759
MEMBRANE_BOUND_VESICLE	112	0.1	1.1	0.341	0.68211	1	10038
LEUKOCYTE_ACTIVATION	67	0.1	1.1	0.348	0.68296	1	13078
MYOFIBRIL	19	0.2	1.1	0.341	0.68065	1	11457
DNA_DAMAGE_RESPONSESIGNAL_TRANSDU	34	0.2	1.1	0.357	0.68062	1	5166
AUXILIARY_TRANSPORT_PROTEIN_ACTIVITY	25	0.2	1.1	0.371	0.68665	1	10497
COENZYME_BINDING	16	0.2	1.1	0.355	0.68682	1	11823
NEURON_PROJECTION	20	0.2	1.1	0.338	0.68529	1	10028
PROTEIN_COMPLEX_ASSEMBLY	162	0.1	1.1	0.345	0.68581	1	8750
POSITIVE_REGULATION_OF_CATALYTIC_ACT	159	0.1	1.1	0.355	0.68629	1	13576
APOPTOTIC_NUCLEAR_CHANGES	18	0.2	1.1	0.34	0.68816	1	10241
VASCULATURE_DEVELOPMENT	54	0.1	1.1	0.347	0.68621	1	10542
DEVELOPMENTAL_MATURATION	18	0.2	1.1	0.372	0.6904	1	6257
INDUCTION_OF_APOPTOSIS_BY_EXTRACELL	25	0.2	1.1	0.355	0.69038	1	5460
BRAIN_DEVELOPMENT	51	0.1	1.1	0.369	0.69056	1	12286
AMINE_RECEPTOR_ACTIVITY	34	0.2	1.1	0.357	0.69454	1	13192
CONDENSED_NUCLEAR_CHROMOSOME	18	0.2	1.1	0.37	0.69568	1	11251
CYTOKINE_SECRETION	18	0.2	1.1	0.369	0.70222	1	13329
ANTIGEN_BINDING	22	0.2	1	0.374	0.71906	1	11455
ORGANELLE_OUTER_MEMBRANE	23	0.2	1	0.388	0.71905	1	3826
MICROTUBULE_ASSOCIATED_COMPLEX	46	0.1	1	0.387	0.72054	1	15350
NUCLEAR_MEMBRANE_PART	42	0.1	1	0.378	0.72272	1	9992
PHOSPHOINOSITIDE_METABOLIC_PROCESS	30	0.2	1	0.375	0.72421	1	1358
POSITIVE_REGULATION_OF_TRANSLATION	34	0.1	1	0.382	0.73133	1	6893
MITOCHONDRIAL_OUTER_MEMBRANE	17	0.2	1	0.398	0.73579	1	2571
NEGATIVE_REGULATION_OF_CELL_ADHESIO	17	0.2	1	0.41	0.74311	1	3653
BASEMENT_MEMBRANE	37	0.1	1	0.413	0.74309	1	8644
RIBOSOMAL_SUBUNIT	20	0.2	1	0.422	0.74111	1	10077
REGULATION_OF_HEART_CONTRACTION	25	0.2	1	0.4	0.73908	1	8489
ANTI_APOPTOSIS	117	0.1	1	0.425	0.73689	1	10921
NEGATIVE_REGULATION_OF_MAP_KINASE_	17	0.2	1	0.444	0.74404	1	13312
NUCLEAR_ORGANIZATION_AND_BIOGENESI	29	0.2	1	0.435	0.74712	1	10241
REGULATION_OF_LYMPHOCYTE_ACTIVATIO	34	0.1	1	0.419	0.7503	1	7478
CYTOKINE_AND_CHEMOKINE_MEDIATED_SI	22	0.2	1	0.447	0.75125	1	5849
MITOCHONDRIAL_ENVELOPE	93	0.1	1	0.428	0.75097	1	10078
VACUOLE	69	0.1	1	0.436	0.75789	1	10703
POSITIVE_REGULATION_OF_TRANSFERASE_	81	0.1	1	0.453	0.76068	1	12339
CYTOKINE_BIOSYNTHETIC_PROCESS	41	0.1	1	0.405	0.76078	1	6893
DNA_DEPENDENT_ATPASE_ACTIVITY	22	0.2	1	0.438	0.75894	1	9171
POSITIVE_REGULATION_OF_TRANSCRIPTION	144	0.1	1	0.44	0.76167	1	6743
SH2_DOMAIN_BINDING	15	0.2	1	0.417	0.76607	1	13015
DETECTION_OF_EXTERNAL_STIMULUS	21	0.2	1	0.422	0.76742	1	14811
MUSCLE_CELL_DIFFERENTIATION	22	0.2	1	0.431	0.77142	1	11551
PEROXISOME_ORGANIZATION_AND_BIOGE	16	0.2	1	0.446	0.77182	1	9723
NUCLEAR_PORE	31	0.2	1	0.427	0.7764	1	13031
MEIOTIC_CELL_CYCLE	35	0.1	1	0.416	0.77635	1	6723
CAMP_MEDIATED_SIGNALING	65	0.1	1	0.476	0.78161	1	13688
TRANSCRIPTION_INITIATION_FROM_RNA_P	29	0.2	1	0.47	0.78971	1	4111
MONOVALENT_INORGANIC_CATION_TRANS	33	0.1	1	0.465	0.78991	1	3445
SPECIFIC_RNA_POLYMERASE_II_TRANSCRIPT	35	0.1	1	0.444	0.79534	1	6280
GLYCEROPHOSPHOLIPID_METABOLIC_PROC	45	0.1	1	0.457	0.80076	1	1358
G_PROTEIN_SIGNALING_COUPLED_TO_CAM	64	0.1	1	0.474	0.80029	1	13688
NEGATIVE_REGULATION_OF_PROGRAMME	150	0.1	1	0.473	0.80073	1	7925
PORE_COMPLEX	36	0.1	1	0.482	0.80869	1	13108
REGULATION_OF_MULTICELLULAR_ORGANI	149	0.1	1	0.449	0.80644	1	13934
AEROBIC_RESPIRATION	15	0.2	1	0.489	0.80664	1	14345
CHROMATIN_BINDING	32	0.1	1	0.498	0.80442	1	11514
OUTER_MEMBRANE	24	0.2	1	0.487	0.81371	1	3826
LEADING_EDGE	47	0.1	1	0.484	0.81308	1	12928
REGULATION_OF_CYTOKINE_SECRETION	16	0.2	1	0.508	0.81319	1	13329
DNA_REPLICATION_INITIATION	15	0.2	1	0.479	0.81186	1	4730
NUCLEAR_BODY	31	0.1	1	0.501	0.81091	1	3193
NEUROTRANSMITTER_RECEPTOR_ACTIVITY	49	0.1	1	0.493	0.81297	1	13059

VIRAL_GENOME_REPLICATION	21	0.2	1	0.498	0.81122	1	11514
RHO_PROTEIN_SIGNAL_TRANSDUCTION	38	0.1	1	0.517	0.81456	1	11457
OXIDOREDUCTASE_ACTIVITY_ACTING_ON_T	22	0.2	1	0.477	0.81451	1	12639
PROTEIN_COMPLEX_BINDING	53	0.1	0.9	0.493	0.81539	1	8224
STEROID_BIOSYNTHETIC_PROCESS	23	0.2	0.9	0.511	0.81484	1	10426
VESICLE	119	0.1	0.9	0.503	0.81338	1	10038
ESTABLISHMENT_AND_OR_MAINTENANCE_	17	0.2	0.9	0.502	0.81724	1	13517
NEGATIVE_REGULATION_OF_APOPTOSIS	149	0.1	0.9	0.5	0.81694	1	7925
PROTEIN_BINDING_BRIDGING	57	0.1	0.9	0.501	0.8158	1	7657
REGULATION_OF_NEUROTRANSMITTER_LEV	24	0.2	0.9	0.513	0.81562	1	11412
STRIATED_MUSCLE_DEVELOPMENT	40	0.1	0.9	0.481	0.81366	1	11714
NEGATIVE_REGULATION_OF_TRANSCRIPTIO	186	0.1	0.9	0.496	0.81364	1	7764
CELL_PROJECTION_PART	19	0.2	0.9	0.517	0.81172	1	10038
RAS_GTPASE_ACTIVATOR_ACTIVITY	29	0.2	0.9	0.514	0.81119	1	14108
NEGATIVE_REGULATION_OF_TRANSCRIPTIO	15	0.2	0.9	0.526	0.80935	1	5970
REGULATION_OF_ORGANELLE_ORGANIZATI	38	0.1	0.9	0.501	0.81762	1	10046
CARBOHYDRATE_METABOLIC_PROCESS	177	0.1	0.9	0.505	0.81563	1	6146
ACETYLTRANSFERASE_ACTIVITY	25	0.2	0.9	0.537	0.81522	1	10931
NUCLEAR_TRANSPORT	86	0.1	0.9	0.516	0.81464	1	13356
GLUCOSE_METABOLIC_PROCESS	28	0.1	0.9	0.51	0.81736	1	6387
CYTOSKELETON_DEPENDENT_INTRACELLUL	25	0.2	0.9	0.503	0.81617	1	9438
RESPONSE_TO_EXTRACELLULAR_STIMULUS	32	0.1	0.9	0.514	0.81504	1	7115
PROTEOGLYCAN_BIOSYNTHETIC_PROCESS	15	0.2	0.9	0.533	0.81548	1	3735
PRIMARY_ACTIVE_TRANSMEMBRANE_TRAN	40	0.1	0.9	0.537	0.81664	1	12227
ESTABLISHMENT_OF_PROTEIN_LOCALIZATI	185	0.1	0.9	0.548	0.81972	1	13439
MACROMOLECULAR_COMPLEX_DISASSEMB	15	0.2	0.9	0.536	0.82215	1	8521
MUSCLE_DEVELOPMENT	93	0.1	0.9	0.537	0.82402	1	12868
RESPONSE_TO_LIGHT_STIMULUS	43	0.1	0.9	0.532	0.82659	1	7106
NEUROTRANSMITTER_BINDING	52	0.1	0.9	0.562	0.82525	1	14752
UBIQUITIN_LIGASE_COMPLEX	26	0.2	0.9	0.529	0.82877	1	2841
ACTIVATION_OF_MAPK_ACTIVITY	37	0.1	0.9	0.545	0.82734	1	10386
POSITIVE_REGULATION_OF_MAP_KINASE_A	42	0.1	0.9	0.549	0.83135	1	8552
NUCLEAR_MEMBRANE	50	0.1	0.9	0.556	0.83351	1	7056
NUCLEOCYTOPLASMIC_TRANSPORT	85	0.1	0.9	0.565	0.83663	1	13356
REGULATION_OF_G_PROTEIN_COUPLED_RE	22	0.2	0.9	0.561	0.83624	1	2011
SULFOTRANSFERASE_ACTIVITY	27	0.1	0.9	0.575	0.83414	1	13403
NEGATIVE_REGULATION_OF_CELLULAR_CO	26	0.1	0.9	0.556	0.83508	1	5685
MAPKKK_CASCADE_GO_0000165	97	0.1	0.9	0.548	0.83301	1	12166
ATPASE_ACTIVITY_COUPLED_TO_MOVEME	40	0.1	0.9	0.559	0.8316	1	15018
POSITIVE_REGULATION_OF_CYTOKINE_PRO	15	0.2	0.9	0.561	0.83892	1	13356
ENZYME_ACTIVATOR_ACTIVITY	120	0.1	0.9	0.576	0.83843	1	14108
MEMBRANE_ORGANIZATION_AND_BIOGEN	133	0.1	0.9	0.582	0.84046	1	8455
REGULATION_OF_INTRACELLULAR_TRANSP	25	0.1	0.9	0.557	0.83836	1	14706
CHANNEL_REGULATOR_ACTIVITY	23	0.2	0.9	0.574	0.8387	1	10497
NEGATIVE_REGULATION_OF_BINDING	18	0.2	0.9	0.594	0.84289	1	5970
CYSTEINE_TYPE_ENDOPEPTIDASE_ACTIVITY	40	0.1	0.9	0.587	0.84128	1	12289
CALCIUM_MEDIATED_SIGNALING	16	0.2	0.9	0.579	0.84909	1	14699
REGULATION_OF_MITOSIS	40	0.1	0.9	0.607	0.84761	1	2384
POSITIVE_REGULATION_OF_RNA_METABOL	120	0.1	0.9	0.618	0.84665	1	12472
N_ACETYLTRANSFERASE_ACTIVITY	21	0.2	0.9	0.593	0.84482	1	12537
PROTEIN_POLYMERIZATION	18	0.2	0.9	0.582	0.84703	1	9916
EXONUCLEASE_ACTIVITY	19	0.2	0.9	0.595	0.85414	1	6462
MITOTIC_CELL_CYCLE_CHECKPOINT	21	0.2	0.9	0.613	0.85689	1	3106
RUFFLE	31	0.1	0.9	0.58	0.85607	1	13333
APICAL_PART_OF_CELL	16	0.2	0.9	0.612	0.85644	1	11431
HYDROLASE_ACTIVITY_ACTING_ON_ACID_A	39	0.1	0.9	0.602	0.85632	1	12227
CARBOHYDRATE_TRANSPORT	18	0.2	0.9	0.618	0.85482	1	8916
RAS_GTPASE_BINDING	25	0.1	0.9	0.593	0.8529	1	6076
HORMONE_METABOLIC_PROCESS	31	0.1	0.9	0.591	0.85385	1	6405
RHO_GTPASE_ACTIVATOR_ACTIVITY	19	0.2	0.9	0.594	0.85766	1	14108
CARBOHYDRATE_BIOSYNTHETIC_PROCESS	49	0.1	0.9	0.608	0.85622	1	6576
SYNAPSE	27	0.1	0.9	0.632	0.85682	1	15548
ORGANELLAR_RIBOSOME	22	0.2	0.9	0.596	0.85554	1	15293
EXTRACELLULAR_MATRIX_PART	56	0.1	0.9	0.626	0.85387	1	8224
GOLGI_MEMBRANE	43	0.1	0.9	0.631	0.85778	1	12247
POSITIVE_REGULATION_OF_SECRETION	20	0.2	0.9	0.619	0.85654	1	15086
SKELETAL_MUSCLE_DEVELOPMENT	31	0.1	0.9	0.615	0.85758	1	11688
SULFURIC_ESTER_HYDROLASE_ACTIVITY	16	0.2	0.9	0.614	0.85584	1	3555
CYTOSKELETAL_PROTEIN_BINDING	156	0.1	0.9	0.638	0.86044	1	11222
INTERPHASE_OF_MITOTIC_CELL_CYCLE	62	0.1	0.9	0.627	0.85958	1	4730
MITOCHONDRIAL_TRANSPORT	20	0.2	0.9	0.63	0.86588	1	10720

SH3_SH2_ADAPTOR_ACTIVITY	41	0.1	0.9	0.647	0.86645	1	7657
RESPONSE_TO_NUTRIENT	17	0.2	0.9	0.7	0.8654	1	13897
T_CELL_ACTIVATION	42	0.1	0.8	0.66	0.87279	1	13078
MITOCHONDRIAL_RIBOSOME	22	0.2	0.8	0.659	0.8726	1	15293
PHOSPHOLIPID_BINDING	44	0.1	0.8	0.671	0.87248	1	14072
CALMODULIN_BINDING	25	0.1	0.8	0.646	0.873	1	6870
NEURON_DEVELOPMENT	59	0.1	0.8	0.661	0.87159	1	13622
CYTOPLASMIC_VESICLE_PART	26	0.1	0.8	0.679	0.87114	1	10007
DRUG_BINDING	16	0.2	0.8	0.644	0.87094	1	10369
GOLGI_ASSOCIATED_VESICLE	27	0.1	0.8	0.651	0.87243	1	8997
SERINE_TYPE_ENDOPEPTIDASE_INHIBITOR_	24	0.1	0.8	0.645	0.87066	1	5680
N_ACYLTRANSFERASE_ACTIVITY	24	0.1	0.8	0.642	0.87159	1	10931
PROTEIN_TRANSPORT	152	0.1	0.8	0.671	0.87212	1	14421
REGULATION_OF_MAPKKK_CASCADE	17	0.2	0.8	0.663	0.87021	1	6490
CYTOPLASMIC_VESICLE_MEMBRANE	26	0.1	0.8	0.69	0.87118	1	10007
REGULATION_OF_BINDING	56	0.1	0.8	0.661	0.8769	1	10249
GLYCEROPHOSPHOLIPID_BIOSYNTHETIC_PR	29	0.1	0.8	0.626	0.87701	1	1358
VESICULAR_FRACTION	44	0.1	0.8	0.678	0.87883	1	13743
SECRETION_BY_CELL	113	0.1	0.8	0.659	0.88034	1	11757
CELLULAR_COMPONENT_DISASSEMBLY	32	0.1	0.8	0.683	0.88073	1	10241
REGULATION_OF_ANATOMICAL_STRUCTUR	24	0.1	0.8	0.647	0.87922	1	10253
PROTEIN_DNA_COMPLEX_ASSEMBLY	48	0.1	0.8	0.673	0.88255	1	6484
STRUCTURE_SPECIFIC_DNA_BINDING	54	0.1	0.8	0.685	0.88151	1	5978
INNATE_IMMUNE_RESPONSE	23	0.1	0.8	0.672	0.88198	1	11611
RNA_EXPORT_FROM_NUCLEUS	20	0.1	0.8	0.702	0.88135	1	10855
POSITIVE_REGULATION_OF_TRANSCRIPTION	118	0.1	0.8	0.679	0.88144	1	12472
SECRETORY_PATHWAY	81	0.1	0.8	0.713	0.88046	1	11757
REGULATION_OF_IMMUNE_EFFECTOR_PRO	15	0.2	0.8	0.702	0.88204	1	13672
NEGATIVE_REGULATION_OF_MULTICELLULA	30	0.1	0.8	0.701	0.88321	1	13934
EXTRACELLULAR_STRUCTURE_ORGANIZATIO	30	0.1	0.8	0.717	0.88776	1	6218
RESPONSE_TO_NUTRIENT_LEVELS	29	0.1	0.8	0.687	0.88804	1	13897
REGULATION_OF_JNK_ACTIVITY	17	0.2	0.8	0.699	0.89413	1	3428
G1_PHASE	15	0.2	0.8	0.715	0.89299	1	12584
ALCOHOL_METABOLIC_PROCESS	87	0.1	0.8	0.72	0.89134	1	14478
REGULATION_OF_RAS_PROTEIN_SIGNAL_TR	19	0.2	0.8	0.699	0.8894	1	11457
HYDROGEN_ION_TRANSMEMBRANE_TRANS	27	0.1	0.8	0.706	0.88886	1	15057
PROTEASE_INHIBITOR_ACTIVITY	40	0.1	0.8	0.686	0.889	1	5680
HISTONE_ACETYLTRANSFERASE_ACTIVITY	16	0.2	0.8	0.709	0.88795	1	3763
RESPONSE_TO_RADIATION	56	0.1	0.8	0.728	0.88786	1	7106
TRANSCRIPTION_FACTOR_COMPLEX	89	0.1	0.8	0.701	0.88739	1	11093
REGULATION_OF_TRANSPORT	67	0.1	0.8	0.687	0.88646	1	14706
PROTEIN_DOMAIN_SPECIFIC_BINDING	70	0.1	0.8	0.703	0.88467	1	11424
JNK_CASCADE	42	0.1	0.8	0.717	0.88566	1	11876
ANTIOXIDANT_ACTIVITY	17	0.2	0.8	0.71	0.88476	1	10921
PROTEIN_KINASE_INHIBITOR_ACTIVITY	24	0.1	0.8	0.719	0.88543	1	12584
SH3_DOMAIN_BINDING	15	0.2	0.8	0.719	0.88411	1	10177
DNA_HELICASE_ACTIVITY	24	0.1	0.8	0.732	0.88721	1	5842
REGULATION_OF_TRANSLATIONAL_INITIATI	28	0.1	0.8	0.714	0.88865	1	10633
ATPASE_ACTIVITY_COUPLED_TO_TRANSME	20	0.1	0.8	0.721	0.88688	1	7303
CELL_SURFACE	77	0.1	0.8	0.733	0.88777	1	10371
PROTEIN_TARGETING	108	0.1	0.8	0.726	0.89266	1	13737
GOLGI_VESICLE_TRANSPORT	45	0.1	0.8	0.745	0.90191	1	3433
MEIOTIC_RECOMBINATION	17	0.2	0.8	0.759	0.90579	1	6723
G_PROTEIN_SIGNALING_ADENYLATE_CYCLA	25	0.1	0.8	0.738	0.90454	1	13576
REGULATION_OF_NUCLEOCYTOPLASMIC_TR	22	0.1	0.8	0.78	0.9027	1	14706
ACTIN_FILAMENT_BINDING	25	0.1	0.8	0.737	0.90269	1	1268
ACTIVATION_OF_PROTEIN_KINASE_ACTIVIT	27	0.1	0.8	0.774	0.90395	1	13856
SERINE_TYPE_PEPTIDASE_ACTIVITY	42	0.1	0.8	0.743	0.90933	1	15898
PHOSPHOINOSITIDE_MEDIATED_SIGNALING	48	0.1	0.8	0.77	0.90864	1	14895
REGULATION_OF_GROWTH	55	0.1	0.8	0.752	0.90746	1	15830
POSITIVE_REGULATION_OF_TRANSPORT	23	0.1	0.8	0.738	0.9086	1	14125
SERINE_TYPE_ENDOPEPTIDASE_ACTIVITY	38	0.1	0.8	0.762	0.90906	1	13342
CELL_PROJECTION_BIOGENESIS	24	0.1	0.8	0.79	0.9123	1	14177
INTERPHASE	68	0.1	0.8	0.809	0.9121	1	4730
REGULATION_OF_PROTEIN_STABILITY	19	0.1	0.8	0.748	0.91383	1	15424
SERINE_HYDROLASE_ACTIVITY	43	0.1	0.8	0.79	0.91267	1	15898
RESPONSE_TO_HYPOXIA	27	0.1	0.8	0.748	0.91147	1	9816
ADENYLATE_CYCLASE_ACTIVATION	19	0.1	0.8	0.779	0.91586	1	13576
ATPASE_ACTIVITY_COUPLED_TO_TRANSME	24	0.1	0.8	0.771	0.91546	1	15018
INSULIN_RECEPTOR_SIGNALING_PATHWAY	18	0.1	0.7	0.784	0.91946	1	5433
STRUCTURAL_CONSTITUENT_OF_CYTOSKELE	56	0.1	0.7	0.814	0.92162	1	11410

COATED_VESICLE	43	0.1	0.7	0.78	0.9221	1	10038
MICROSOME	42	0.1	0.7	0.799	0.92711	1	13743
EXTRACELLULAR_MATRIX	96	0.1	0.7	0.803	0.92566	1	8644
INTRACELLULAR_PROTEIN_TRANSPORT	141	0.1	0.7	0.827	0.92604	1	14421
PROTEASOME_COMPLEX	23	0.1	0.7	0.822	0.93292	1	14213
LAMELLIPODIUM	25	0.1	0.7	0.835	0.94027	1	11538
REGULATION_OF_MITOTIC_CELL_CYCLE	23	0.1	0.7	0.822	0.94266	1	4730
GLUTAMATE_RECEPTOR_ACTIVITY	20	0.1	0.7	0.837	0.94085	1	9310
EXTERNAL_SIDE_OF_PLASMA_MEMBRANE	15	0.2	0.7	0.853	0.93907	1	6915
NEGATIVE_REGULATION_OF_PROTEIN_MET	46	0.1	0.7	0.816	0.93934	1	6218
REGULATION_OF_ENDOCYTOSIS	16	0.2	0.7	0.803	0.93798	1	9705
LYMPHOCYTE_DIFFERENTIATION	26	0.1	0.7	0.859	0.94698	1	7651
NEGATIVE_REGULATION_OF_DNA_BINDING	17	0.1	0.7	0.836	0.94537	1	13349
CLATHRIN_COATED_VESICLE	35	0.1	0.7	0.83	0.94599	1	10038
PROTEOLYSIS	184	0	0.7	0.846	0.94442	1	16389
HYDROLASE_ACTIVITY_ACTING_ON_CARBO	21	0.1	0.7	0.869	0.95196	1	14037
POSITIVE_REGULATION_OF_TRANSCRIPTION	65	0.1	0.7	0.843	0.95348	1	6743
G_PROTEIN_SIGNALING_COUPLED_TO_IP3_	45	0.1	0.7	0.874	0.95267	1	14895
NEGATIVE_REGULATION_OF_CELLULAR_PR	44	0.1	0.7	0.872	0.95721	1	6218
NUCLEOBASENUCLEOSIDENUCLEOTIDE_AND	31	0.1	0.7	0.874	0.95571	1	15618
REGULATION_OF_CELL_GROWTH	43	0.1	0.7	0.839	0.95792	1	15642
LEUKOCYTE_DIFFERENTIATION	36	0.1	0.7	0.842	0.95814	1	9296
B_CELL_ACTIVATION	20	0.1	0.7	0.887	0.95855	1	13078
MEIOSIS_I	20	0.1	0.7	0.853	0.95923	1	6723
HOMOPHILIC_CELL_ADHESION	16	0.1	0.7	0.852	0.96349	1	15580
PROTEINACEOUS_EXTRACELLULAR_MATRIX	95	0.1	0.7	0.865	0.96239	1	8644
NEURITE_DEVELOPMENT	51	0.1	0.7	0.877	0.9638	1	11690
PROTEIN_HETERODIMERIZATION_ACTIVITY	76	0.1	0.7	0.888	0.96624	1	10706
MICROTUBULE_BASED_MOVEMENT	15	0.1	0.7	0.842	0.96711	1	9438
TRANSFERASE_ACTIVITY_TRANSFERRING_SU	31	0.1	0.7	0.874	0.96758	1	12185
CYTOKINESIS	18	0.1	0.7	0.889	0.96615	1	12648
RESPONSE_TO_ABIOTIC_STIMULUS	83	0.1	0.7	0.878	0.96752	1	5842
ENDOPEPTIDASE_ACTIVITY	112	0.1	0.7	0.892	0.96641	1	15970
SYNAPTOGENESIS	17	0.1	0.7	0.896	0.96468	1	5005
REGULATION_OF_PROTEIN_IMPORT_INTO_	16	0.1	0.7	0.888	0.96308	1	13349
POSITIVE_REGULATION_OF_HYDROLASE_AC	54	0.1	0.7	0.896	0.96269	1	13329
NUCLEOTIDE_BIOSYNTHETIC_PROCESS	19	0.1	0.7	0.897	0.97066	1	15713
GOLGI_APPARATUS_PART	96	0.1	0.7	0.911	0.97125	1	13300
MEMBRANE_LIPID_METABOLIC_PROCESS	100	0.1	0.7	0.905	0.97201	1	1358
INTRINSIC_TO_GOLGI_MEMBRANE	15	0.1	0.7	0.888	0.97038	1	9489
REGULATION_OF_T_CELL_ACTIVATION	27	0.1	0.6	0.92	0.96952	1	7478
KINASE_REGULATOR_ACTIVITY	44	0.1	0.6	0.933	0.97747	1	14557
SYNAPSE_ORGANIZATION_AND_BIOGENESIS	22	0.1	0.6	0.922	0.97944	1	6218
ADHERENS_JUNCTION	22	0.1	0.6	0.917	0.98185	1	15995
CELLULAR_MORPHOGENESIS_DURING_DIFF	47	0.1	0.6	0.935	0.98224	1	13622
ER_TO_GOLGI_VESICLE_MEDIATED_TRANSP	17	0.1	0.6	0.899	0.98131	1	7280
SKELETAL_DEVELOPMENT	101	0.1	0.6	0.918	0.97966	1	16592
PURINE_RIBONUCLEOTIDE_BINDING	195	0	0.6	0.915	0.97891	1	3196
MEMBRANE_LIPID_BIOSYNTHETIC_PROCESS	48	0.1	0.6	0.927	0.98223	1	7706
ER_GOLGI_INTERMEDIATE_COMPARTMENT	24	0.1	0.6	0.934	0.98058	1	11624
DIGESTION	41	0.1	0.6	0.926	0.97893	1	743
KINASE_INHIBITOR_ACTIVITY	25	0.1	0.6	0.93	0.97784	1	12584
CASPASE_ACTIVATION	25	0.1	0.6	0.915	0.97621	1	3198
INTEGRIN_BINDING	29	0.1	0.6	0.92	0.97506	1	8224
CELL_DIVISION	20	0.1	0.6	0.912	0.97834	1	13285
MYOBLAST_DIFFERENTIATION	17	0.1	0.6	0.949	0.97711	1	11551
ACTIN_FILAMENT_ORGANIZATION	24	0.1	0.6	0.932	0.97619	1	4900
PROTON_TRANSPORTING_TWO_SECTOR_AT	15	0.1	0.6	0.94	0.97476	1	12100
CELL_CYCLE_ARREST_GO_0007050	54	0.1	0.6	0.923	0.97981	1	14463
NEUROPEPTIDE_BINDING	22	0.1	0.6	0.939	0.98189	1	14551
GTPASE_ACTIVATOR_ACTIVITY	58	0.1	0.6	0.948	0.98353	1	15642
LYTIC_VACUOLE	61	0.1	0.6	0.951	0.98297	1	10703
LYSOSOME	61	0.1	0.6	0.95	0.98405	1	10703
ANION_TRANSMEMBRANE_TRANSPORTER_	59	0.1	0.6	0.947	0.98484	1	16917
MORPHOGENESIS_OF_AN_EPITHELIUM	16	0.1	0.6	0.934	0.98421	1	6835
PROTEIN_OLIGOMERIZATION	38	0.1	0.6	0.939	0.98593	1	7616
INTRINSIC_TO_ORGANELLE_MEMBRANE	51	0.1	0.6	0.954	0.98644	1	14372
CELL_PROJECTION	105	0	0.6	0.967	0.98604	1	14304
VESICLE_MEMBRANE	28	0.1	0.6	0.97	0.98474	1	10007
HYDRO_LYASE_ACTIVITY	27	0.1	0.6	0.965	0.98718	1	3734
CELL_SUBSTRATE_ADHERENS_JUNCTION	15	0.1	0.6	0.965	0.98547	1	6270

ACTIN_POLYMERIZATION_AND_OR_DEPOLY	23	0.1	0.6	0.967	0.98464	1	10031
RECEPTOR_MEDIATED_ENDOCYTOSIS	33	0.1	0.6	0.971	0.98433	1	8403
STRESS_ACTIVATED_PROTEIN_KINASE_SIGN	44	0.1	0.6	0.96	0.98307	1	15552
INORGANIC_CATION_TRANSMEMBRANE_TR	57	0.1	0.6	0.969	0.98219	1	15057
NEUROPEPTIDE_RECEPTOR_ACTIVITY	21	0.1	0.6	0.979	0.98096	1	14551
HORMONE_ACTIVITY	43	0.1	0.5	0.984	0.99173	1	10123
T_CELL_DIFFERENTIATION	15	0.1	0.5	0.979	0.99273	1	7651
INTEGRAL_TO_ORGANELLE_MEMBRANE	49	0.1	0.5	0.985	0.99176	1	14372
PROTEIN_SECRETION	32	0.1	0.5	0.988	0.99073	1	13329
REGULATION_OF_CELL_MIGRATION	28	0.1	0.5	0.99	0.99568	1	10254
NUCLEAR_EXPORT	33	0.1	0.4	1	0.99933	1	1649

Table S4 | Top 1000 depleted genes for both A375 and HUES62. Mean depletion for each gene is given as the log2 ratio of Day 14 vs. Day 3 representation (mean over sgRNAs for the gene).

A375		**HUES62**	
gene_name	mean depletion	gene_name	mean depletion
RPS19	-2.882652431	RPS19	-3.183585341
TCOF1	-2.808435977	SUMO1	-2.958691468
NIP7	-2.577017439	IGFN1	-2.816486619
CARS2	-2.524564219	AGAP5	-2.781890338
RPL7	-2.510763424	VOPP1	-2.764536999
ARL17A	-2.452404991	JAKMIP1	-2.722075866
RPS18	-2.360007937	HIST2H2AC	-2.609990396
RPS11	-2.331818955	SPHAR	-2.582311984
RPL32	-2.27812036	LCE3E	-2.525929706
DENR	-2.257042611	PDRG1	-2.499694407
RPL6	-2.23869209	RRP1B	-2.361922343
ADSL	-2.237218508	PFDN4	-2.321026472
DNM2	-2.213359485	OVGP1	-2.294064989
ACTL6A	-2.197447807	CCDC58	-2.290819552
PPAN	-2.178384698	HIST1H2BJ	-2.288803994
NT5C1B-RDH	-2.175777594	CCDC73	-2.279966592
ENO1	-2.17247027	ZSCAN18	-2.277760787
DOLK	-2.140854234	DENR	-2.253261386
ASH2L	-2.137162022	CHKA	-2.231856136
SNRPF	-2.129389793	FAM185A	-2.226396662
RPL26	-2.125670091	OCM	-2.225306785
GABPA	-2.106954316	KBTBD11	-2.2083224
VOPP1	-2.088272162	RPL32	-2.198484015
RSL1D1	-2.077068149	RBMXL2	-2.193406936
RRAGA	-2.075755103	LRRC37A3	-2.188978264
URB1	-2.061968502	SNRPG	-2.180311606
MRP63	-2.058260881	POLR2J	-2.179863073
NAA30	-2.056104946	EID1	-2.177256367
KPNB1	-2.045863711	HMGN4	-2.152073487
RPL39	-2.042789125	FJX1	-2.144074596
EIF2B5	-2.018537107	MRPS18C	-2.143839164
XRN1	-2.007802712	UTP18	-2.13822949
LSM2	-2.006908746	GCSH	-2.123373465
MASP2	-1.996597431	HIST1H2AG	-2.10248405
DEFB131	-1.981628571	MT1E	-2.102441783
LSM7	-1.977614338	RPL30	-2.087694615
NHP2L1	-1.977025309	TMEM52	-2.078628045
RPS15A	-1.964623412	XPA	-2.075701399
EEF1A1	-1.940570892	ARHGEF19	-2.074475526
RBX1	-1.931878232	RAMP2	-2.071163793
PTPMT1	-1.931127795	MTA3	-2.060680607
CCDC146	-1.930330138	POLRMT	-2.058734986
COBRA1	-1.924683023	ZNF524	-2.051959832
VPS25	-1.919175993	RSL24D1	-2.047403722
RPL8	-1.915827854	EXOSC1	-2.036942474
POLR2I	-1.914363716	BATF	-2.035568177
NHP2	-1.908840701	KRTAP11-1	-2.033591989
OR5M3	-1.903054531	FCF1	-2.03040005
SDAD1	-1.898279431	NEUROG1	-2.024122047
DNAJA3	-1.895932148	NSRP1	-2.016177389
IMP4	-1.886050088	XYLT1	-2.013363239
MOAP1	-1.882851477	CNIH4	-2.010919939
NUTF2	-1.873263167	RPS7	-2.005077402
PTPN23	-1.869411288	PLAC9	-1.99787552
RPL14	-1.854061225	DCPS	-1.993526745
RP11-110H1.	-1.838203216	HMGN1	-1.985137369
TPT1	-1.834186561	HIST1H2BM	-1.966034904
COPS3	-1.830313031	RPS11	-1.958203408
HARS	-1.808567224	TP53TG5	-1.952603327
ATP6V0C	-1.806752366	KRT82	-1.951720459
CCNH	-1.802427683	MRP63	-1.950917553
RPL7A	-1.801850968	OR51V1	-1.950395101
COL25A1	-1.789186395	RPL7A	-1.945684794
EEF2	-1.773430832	MTMR1	-1.942316422
EEFSEC	-1.773082367	TMEM144	-1.940658066
LGALS8	-1.772564445	ACSM1	-1.938959493
SFPQ	-1.771314781	RRN3	-1.933600629
EIF2S3	-1.769731164	IPO4	-1.932523341
COPB1	-1.762259717	HNRNPU	-1.929921878
RBMX2	-1.758857017	GTF3C1	-1.924067851
POLR3H	-1.753585716	RPL6	-1.923613883
RPL10	-1.75174146	CCDC90B	-1.916359703
TMLHE	-1.750717975	C15orf42	-1.912360544
TUBG1	-1.749877928	CITED4	-1.912125059
ANKRD30A	-1.74932094	CXCR3	-1.910371663
KCNJ16	-1.74542423	ICOS	-1.907257673
ZNF207	-1.743830295	AKR1A1	-1.904032674
PTRH2	-1.735681069	WDR83OS	-1.902920977
CAPZB	-1.733659665	RMI1	-1.900641673

HNRNPU	-1.732106008	RFC5	-1.894008779
YEATS2	-1.72409334	OR5AR1	-1.888994891
RPL37	-1.72397052	FAM96B	-1.88827946
RPF1	-1.722952482	PCDHB1	-1.887315952
SUMO2	-1.722198581	RPL8	-1.862649576
ACACA	-1.719950822	TTLL4	-1.862595159
CAPZA1	-1.719035764	ELOVL2	-1.858705763
FARSB	-1.707506458	JAG2	-1.853386152
CTDP1	-1.705884315	RBMX2	-1.842871507
SS18L2	-1.70390379	POLR3K	-1.8372641
CENPI	-1.703824885	ZBTB39	-1.834577541
PRPF38B	-1.703372866	PKD1	-1.834139042
SF3B1	-1.702731503	MFSD2A	-1.833483748
MAPK1	-1.69651763	RAE1	-1.833119559
MOCS3	-1.68666595	RIMBP3B	-1.832150575
POP7	-1.685420318	PKN3	-1.831875987
UTP18	-1.684192052	YY1	-1.830589818
ME3	-1.683035372	CWC25	-1.829810575
PSMC2	-1.681322654	ARSE	-1.823179326
TBC1D2B	-1.680850452	NBR1	-1.823032991
MRPL17	-1.678664073	PRNP	-1.815793705
PIGW	-1.676457135	NUDC	-1.81045846
RPL30	-1.674678234	KDM4E	-1.810122958
GFM1	-1.672030725	RBX1	-1.800761527
APPL1	-1.667691292	TSPYL2	-1.800195078
PRAMEF18	-1.661579353	RALGDS	-1.798929091
THOC2	-1.659978325	C14orf80	-1.796756631
DCPS	-1.65488046	APBA3	-1.791344673
RPS21	-1.649662797	ENO1	-1.79011033
POLR2L	-1.647400059	SMG1	-1.784878697
DPPA3	-1.643632209	C9orf169	-1.778113126
PRAMEF11	-1.640377216	ZNRD1	-1.774181477
TBCC	-1.637735404	KCNJ16	-1.769711082
MRPS12	-1.637593143	POLR2I	-1.769423783
EFTUD2	-1.63609533	UBA52	-1.768260354
BEX1	-1.634269725	NOC4L	-1.764945455
NOL6	-1.63270992	HORMAD2	-1.764870613
HNRNPK	-1.631201515	OR9Q2	-1.760481348
SNRNP70	-1.630423532	HPN	-1.75865726
RPL4	-1.628309405	KRT24	-1.758465732
H3F3B	-1.621875698	FOXH1	-1.757242912
MATR3	-1.620666917	GDF9	-1.756109302
RPL38	-1.618433284	CEP290	-1.753803294
PGD	-1.617906932	ADRA2C	-1.753773058
DAP3	-1.616024661	TULP1	-1.749849627
TSR1	-1.612896573	LTBR	-1.749021049
SMC1A	-1.607195432	ZCCHC12	-1.746744432
RPL9	-1.60619161	RPAIN	-1.73474472
RPS12	-1.603986362	B3GALT4	-1.733297288
SNRNP200	-1.597597784	ATP1A2	-1.728486738
ZNRD1	-1.595667827	PCDHB16	-1.728250573
TFAM	-1.592538964	CDAN1	-1.724068055
TLN1	-1.592240013	PIP5K1C	-1.723834562
CHST7	-1.591104236	MPP4	-1.722234521
RFK	-1.589972652	SPOCD1	-1.721697697
VARS	-1.589849258	H3F3B	-1.721342781
WT1	-1.588292311	RPS21	-1.717399432
PDAP1	-1.588174658	BEX1	-1.716075951
WARS2	-1.586972934	DDX41	-1.716023943
OCM	-1.586564929	ATP12A	-1.714599078
TEX14	-1.582436009	PLEKHA6	-1.71359395
OR7C2	-1.580970812	SIGLEC5	-1.711535603
SNAP23	-1.579522004	GPR115	-1.711244409
FURIN	-1.579107358	PGBD4	-1.709127717
C19orf25	-1.576034681	ABCC3	-1.709096583
GNB2L1	-1.57535027	C1QTNF4	-1.704914364
PCF11	-1.573868556	SUZ12	-1.702460494
C6orf226	-1.573804931	IRS1	-1.701590078
DHX15	-1.570412486	POLR1A	-1.7013335
NUP88	-1.567264532	TMEM183A	-1.700220613
EIF2S1	-1.563321294	OR52B4	-1.699496045
PET117	-1.562889941	SLC13A2	-1.699062296
PPP2CA	-1.562824258	TUBGCP3	-1.695027009
CMPK1	-1.557510591	GGT7	-1.690668273
RAE1	-1.553916339	OR1D2	-1.689507147
CIRH1A	-1.55196902	TUBG2	-1.686771713
DDX42	-1.548957925	FOXB1	-1.686159699
POLR3A	-1.54531119	COX4I2	-1.685145656
RPS5	-1.544242565	CFHR5	-1.684484434
RUVBL2	-1.54307586	COX7B2	-1.683824823
KHDRBS1	-1.540530485	ZMYND8	-1.679931871
UBQLN3	-1.539875621	ANKLE2	-1.67977325
SART3	-1.538803977	ZBTB32	-1.677758798
CTU2	-1.532672693	MEX3A	-1.67283445
EXOSC9	-1.53240283	IRF2BPL	-1.66817721

EIF3D	-1.531272229	XPO1	-1.665911185
FOSL1	-1.525912762	SERPINB3	-1.665420952
SKIV2L2	-1.524792166	SPC24	-1.664003074
NSL1	-1.523902984	ZNF835	-1.663591136
PKD2L2	-1.522030203	HSP90AB1	-1.65845304
COX17	-1.521428227	C1orf52	-1.657906239
RAB3GAP1	-1.518439462	EXOSC8	-1.657418649
SBDS	-1.518313565	PPP1R7	-1.654337881
HSD17B10	-1.516651173	ANAPC7	-1.654087519
RPL34	-1.514777041	PDP2	-1.652883515
MRPL41	-1.514148656	LRRC6	-1.649462528
KIF23	-1.511701917	PCDHGC5	-1.641146446
BRIP1	-1.510169164	ECH1	-1.637984733
PSMA3	-1.50978052	BIRC6	-1.635174985
MYO18A	-1.506084393	CHMP4C	-1.631396522
OR5K3	-1.501361245	URB1	-1.628023834
PCNA	-1.500086419	PPP4C	-1.626848674
COX4I1	-1.495514571	LRRC3	-1.624158807
CCDC23	-1.491525997	FAM207A	-1.623564041
SLC26A7	-1.491379231	TSSK1B	-1.623386054
GJA3	-1.490625294	SNRNP35	-1.622193825
PMF1	-1.489084741	ENTPD7	-1.621420381
ZNF259	-1.488562555	ZNF559	-1.619457887
ARHGAP11A	-1.487361831	PLEKHA3	-1.619359014
INTS8	-1.485702565	PSMB11	-1.619357614
COX5B	-1.483628484	C12orf57	-1.6192204
BCL2L2-PABF	-1.479334824	BCL9L	-1.616431663
ATP6AP2	-1.476781098	COL6A2	-1.616189888
FNTB	-1.473951658	PHLDA2	-1.616178629
MTA3	-1.473861711	ERAS	-1.613501381
TDRD10	-1.473540335	GAS8	-1.611441409
TSG101	-1.472472944	ANAPC1	-1.609927961
HSP90B1	-1.472220581	PHIP	-1.606091841
KIF2A	-1.471850262	TMEM234	-1.605376698
MED14	-1.469852205	RPL13A	-1.603258551
ANKRD49	-1.469829543	USP44	-1.601487248
PSMB4	-1.468797099	HNRNPA0	-1.601341264
COX5A	-1.467673157	COX6B1	-1.598937125
PCBP1	-1.465993867	KRTCAP2	-1.597973049
FCF1	-1.465773243	CASKIN1	-1.597967074
TINF2	-1.465625197	IFNB1	-1.588890032
LAMTOR3	-1.461323319	MED21	-1.588539266
RPL11	-1.459385197	SDSL	-1.588435672
MDM2	-1.457827281	RPS6	-1.587775088
CTNNBL1	-1.45731148	DDX42	-1.587535926
RPL15	-1.457245851	LIN7C	-1.587142859
SOX10	-1.457045107	UBXN4	-1.587070505
TUBGCP3	-1.455922895	DSN1	-1.582628585
KDSR	-1.45079145	NTAN1	-1.581097107
HSPA8	-1.44920478	CDC26	-1.580081851
MAD2L1	-1.448620304	PIGM	-1.578178236
ZFHX3	-1.447869343	CHD6	-1.577282235
DYNLL1	-1.446908968	CHORDC1	-1.574916503
C17orf81	-1.444492658	UVRAG	-1.573957952
NGDN	-1.444452376	ZNF580	-1.572557983
CENPC1	-1.444330973	OR4D10	-1.570303265
POLR3K	-1.444320245	COG6	-1.569988804
KRI1	-1.443946118	FBXO41	-1.567074156
DNAJB1	-1.443734639	C1orf150	-1.566762543
SLC35C2	-1.442854155	MMP23B	-1.56595931
SAE1	-1.437585047	FFAR3	-1.562720247
NR1I3	-1.437194199	PIGW	-1.562033012
NKAP	-1.436957722	ZRSR2	-1.560314358
TBCA	-1.436566244	ARMC7	-1.56023241
CABIN1	-1.434611745	EIF6	-1.558951618
HJURP	-1.433849464	ANKRD49	-1.55887604
TRMT112	-1.433490187	PIK3CA	-1.558845668
ZNF529	-1.432525336	DEFB131	-1.55797361
RPS27A	-1.432347982	CLDN4	-1.550420395
ARMC7	-1.429603057	C5orf62	-1.548815903
AGAP6	-1.429039924	C7	-1.548712647
POLR1B	-1.428651863	COPB1	-1.548302258
FAM96B	-1.427271021	STX18	-1.547594206
PMVK	-1.42708923	MASP2	-1.545823489
CSNK2B	-1.426586006	RP11-528L24.3	-1.545098873
KPNA4	-1.426305655	PEX16	-1.544210673
RPL13	-1.425968515	TMCC3	-1.542308989
RPL35A	-1.425528555	FTSJD1	-1.54122008
CUL1	-1.425420937	PDF	-1.540774209
SUPT6H	-1.424775226	TSR1	-1.537975442
RPS3	-1.424672812	WWC2	-1.535385295
RRP1	-1.424495031	EIF4E1B	-1.535041313
SF1	-1.422731301	PCDHB7	-1.534750337
IL9	-1.422056509	ASNS	-1.533747699
BUB1	-1.421531126	GNG7	-1.533427432

YY1	-1.419062109	RBM48	-1.531893314
SMARCA5	-1.416042074	HIST2H2BE	-1.530781789
PSMD12	-1.415969492	CGB1	-1.530628903
RANBP1	-1.415302054	S100A11	-1.529786068
PSMB1	-1.415056441	EIF5	-1.52717872
WDR74	-1.414139191	DGCR8	-1.52706625
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BUD31	-1.413072743	PI4K2A	-1.52350573
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PPA1	-1.410634008	SGTA	-1.519321666
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NOC4L	-1.409986802	POTED	-1.517539425
CCDC59	-1.409761529	PSME3	-1.514880312
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POLR2E	-1.408878942	LCN8	-1.513494042
DGCR8	-1.406358064	CDC42BPB	-1.512815457
TOR1AIP1	-1.406117404	PA2G4	-1.511632954
EXOSC5	-1.405249481	PLEKHH1	-1.510365559
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USP1	-1.403615672	TFAM	-1.509576181
ANAPC7	-1.401430164	ATP6V0C	-1.508572478
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GAPDH	-1.400273726	MEIS1	-1.506671145
ST13	-1.398019204	PRDM14	-1.505804106
CCDC73	-1.394548173	QRFP	-1.504909604
TERF2	-1.394231255	BRAT1	-1.504170191
NOL12	-1.391253457	WDR76	-1.502637608
DBR1	-1.390682155	VWDE	-1.499084118
RBBP5	-1.390436818	KLHL34	-1.497309165
CASC5	-1.390361403	ALLC	-1.497016423
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ISCA2	-1.38933325	CTU1	-1.496320563
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PRKRIR	-1.382824438	KRT13	-1.49155935
UBC	-1.382750556	CLUL1	-1.491275178
CHTF8	-1.38225867	PSMB3	-1.490755153
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SPATA5	-1.371546126	USP43	-1.47642241
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GTPBP4	-1.363346727	EID2B	-1.468609431
TRAPPC4	-1.363085076	GSTZ1	-1.468284552
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EIF6	-1.35358833	NOL3	-1.46141808
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CINP	-1.349546146	OR5K3	-1.458559144
PES1	-1.348241514	HOXA5	-1.458453821
EIF1AD	-1.347681684	ARL17A	-1.457715258
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CLEC10A	-1.346590066	TBL3	-1.455849732
POLR2D	-1.344792099	RNF20	-1.455503496
EIF1	-1.344559124	TBCA	-1.455477108

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TAF3	-1.340156516	BCAS2	-1.451342376
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PPA2	-1.335089026	GARS	-1.449537798
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NDUFB10	-1.332788339	TFPT	-1.447926352
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MED21	-1.330290534	TCTEX1D2	-1.446558259
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SCO2	-1.329754225	VPS13C	-1.445038424
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DIMT1	-1.317151465	DNAJC11	-1.435812507
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C11orf75	-1.308307405	EXOSC7	-1.431428179
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PRRG4	-1.304157843	GPR124	-1.426512806
SFXN4	-1.303922126	DLL3	-1.422088402
DHX8	-1.302999971	C10orf131	-1.421588642
SMC2	-1.302938995	ATF5	-1.420593385
ACY1	-1.302662808	KRTAP19-4	-1.420517301
GPN3	-1.298923505	PRODH	-1.41981364
SOCS3	-1.298536471	C21orf59	-1.419547323
NTN4	-1.296514333	LCE3D	-1.418646134
UTP14A	-1.296499694	CRH	-1.418237482
CHORDC1	-1.295389856	BCL2L1	-1.418154714
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CERS1	-1.28449224	DESI1	-1.408796498
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ABHD11	-1.273190504	EIF2C2	-1.402259615
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GABPB1	-1.269810752	KRTAP4-2	-1.400786406
HIVEP3	-1.269565848	NT5DC1	-1.400673886
BRD2	-1.267679421	RPS27A	-1.399937957
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BUB3	-1.26667183	NAA30	-1.399482582
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PSMG3	-1.257309475	GLS2	-1.391718029
METTL14	-1.256067935	ADM2	-1.391549928
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PLDN	-1.254998982	RFC3	-1.391106035

EIF2S2	-1.253613636	HIST1H1B	-1.390959146
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ELMOD3	-1.249168045	PCDH18	-1.386154855
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EIF3A	-1.247652565	NSUN5	-1.384773039
GPN1	-1.246678919	C5orf55	-1.384724887
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VMP1	-1.245973445	SGCA	-1.384606557
C5orf62	-1.245529521	CIRH1A	-1.383945728
ENTHD1	-1.245322091	ACTR6	-1.38346989
C7orf23	-1.245093698	FNBP4	-1.383464816
ANAPC4	-1.243819302	SAFB	-1.382666602
C20orf111	-1.242250028	ZXDC	-1.381995699
FAM118B	-1.240759583	HAUS1	-1.381551871
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ASXL3	-1.24012825	C3orf71	-1.381187345
COPB2	-1.240117622	NAALAD2	-1.380921778
REV3L	-1.239474867	LGALS3BP	-1.379993411
EMC7	-1.237474252	SMURF2	-1.378588024
PGP	-1.237066107	FGF17	-1.378469131
ACTR6	-1.237008101	DLG5	-1.378430761
CNPY2	-1.236908843	SAE1	-1.377958941
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POLE2	-1.235250832	DUOX1	-1.373580298
PHTF2	-1.234956081	MOCS3	-1.373232039
SERAC1	-1.234566406	CRYGC	-1.371555233
SOD2	-1.234331381	MED1	-1.370418999
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RFC3	-1.233260688	C1D	-1.370106538
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POLR1A	-1.232242665	VTN	-1.368899379
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COG1	-1.229778648	COX6B2	-1.367659662
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PKM	-1.223253054	TXLNG	-1.365995186
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CDK9	-1.216810421	RANBP1	-1.359068915
TRMT6	-1.214842285	PIGS	-1.359026633
EIF4E	-1.214767047	ARL4D	-1.358847203
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HEATR1	-1.212823082	PARM1	-1.358529964
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TRIAP1	-1.211850501	TMEM97	-1.357995121
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MIOS	-1.203407099	CATSPERB	-1.352848215
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VAC14	-1.200270595	CTTNBP2NL	-1.350201785
COASY	-1.199434983	PSMC2	-1.34990278
TPR	-1.199227411	CEP250	-1.349774107
IGBP1	-1.194961933	CD70	-1.349522814
DIS3	-1.193716642	NKAIN1	-1.349086317
CRKL	-1.193291148	TRIM61	-1.34874964
IL36G	-1.192801712	BRI3	-1.348477965
CUL2	-1.192688233	BTF3L4	-1.346826486
POLRMT	-1.192245098	SART3	-1.345977605
GCSH	-1.191032683	LSS	-1.345250492
PDRG1	-1.190777209	NDUFA7	-1.344087552
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C11orf10	-1.187078268	TTC30A	-1.340200386
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AP2B1	-1.183349851	TRIAP1	-1.339070801
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LAS1L	-1.182768104	YIPF3	-1.338477848
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RPAP3	-1.174222309	TCHHL1	-1.331605136
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BCAS2	-1.169813503	RPL10	-1.330485089
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GINS3	-1.168900802	PSMA6	-1.329932606
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C12orf50	-1.163923228	ACTL6A	-1.324089056
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CCT6A	-1.161600828	SNRPF	-1.322855177
CNIH4	-1.161143723	CCR7	-1.322225566
VCL	-1.160033322	PADI4	-1.322023506
TIPRL	-1.159975204	RBPMS	-1.321787351
EXOSC1	-1.159391695	SLC38A5	-1.321627333
GINS2	-1.159330215	ASH2L	-1.321380735
POLR2G	-1.159291555	C11orf87	-1.320546465
SMU1	-1.158961843	USP3	-1.319967007
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ATP10B	-1.155904663	ZBTB34	-1.319356965
EIF5A	-1.155231855	PDE6C	-1.318981816
PSMD14	-1.15495698	C15orf63	-1.318881749
TARS	-1.154929744	SUSD3	-1.318679868
SIAE	-1.154924856	TUBG1	-1.318445333
CIAO1	-1.152202616	CPSF4L	-1.317067473
VPS4A	-1.151884009	RBM28	-1.316596094
RBBP6	-1.151745314	EEF2	-1.315436524
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MAP3K2	-1.148652316	39880	-1.310145651
RQCD1	-1.148569283	SH3TC1	-1.309541761
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TMED3	-1.147828583	C11orf35	-1.307697103
PRPF4	-1.147629016	DNAJC17	-1.307558425
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CCT8	-1.137811964	EID2	-1.305751897
ACO2	-1.137710016	UBL4B	-1.304917945
MFAP1	-1.13741397	KDM1A	-1.304656676
FERMT2	-1.136351485	BHLHA9	-1.304141607
S100G	-1.136310018	MEF2BNB	-1.303573291
FXN	-1.135711566	PPFIA4	-1.303480594
NME5	-1.13560789	SLC4A1	-1.303428597
KLF1	-1.135604126	CNPY2	-1.302819574
EIF3B	-1.135426481	GPR85	-1.302577615
SLC35D1	-1.135048079	C17orf81	-1.301560659
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FAM185A	-1.133299596	LMOD3	-1.299696123
YARS2	-1.132928814	TDO2	-1.298072075
VN1R2	-1.132829488	SRSF7	-1.297876366
SETDB1	-1.132566535	H2BFM	-1.297338338
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ANAPC1	-1.127929837	WDR88	-1.295032877
C16orf72	-1.126826866	DSC3	-1.295010072
WWTR1	-1.126787364	GJA9	-1.293636712
CEBPZ	-1.126574933	TCFL5	-1.293523283
TCEB2	-1.124750634	C3orf25	-1.293387208
NDUFA2	-1.124713541	CCL13	-1.29259661
STX5	-1.124386769	BEGAIN	-1.292257661
RPL5	-1.123550445	DUSP21	-1.291745466
U2AF1L4	-1.12303907	TBX5	-1.291047766
FARSA	-1.122975506	GTPBP4	-1.290879142
MAT2A	-1.12249972	FBXW4	-1.290656771
CCDC101	-1.12247241	TRAF3IP3	-1.289221532
NBR1	-1.122159404	LAIR2	-1.289006794
S100PBP	-1.120559064	CCDC17	-1.288946689
PSMD2	-1.120410134	NSUN6	-1.288379213
CIT	-1.12012829	HSD17B7	-1.287990136
TUBGCP4	-1.119913794	SIGLEC15	-1.286365988
POLG2	-1.119353373	YPEL1	-1.285892981
MASTL	-1.119162982	C12orf71	-1.284890782
PSMC5	-1.116680643	RPS18	-1.284861476
TRA2B	-1.116641119	PAQR3	-1.284117989
FUS	-1.115787787	PRPF6	-1.283508664
LMLN	-1.115653475	HSPA8	-1.283421376
XRCC4	-1.115385414	PLS1	-1.283356689
XPO1	-1.115279503	FXYD7	-1.283150611
KRTCAP2	-1.113876033	OR10A7	-1.283133705
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RRP1B	-1.11248171	PRRC2A	-1.28242491
SLC25A3	-1.111489522	NDNL2	-1.281118975
TCP1	-1.111045616	SYNGR2	-1.280972586
TNFSF12-TNF	-1.110535589	ADO	-1.280890515
PHF5A	-1.110430938	C7orf50	-1.280705584
ACTR2	-1.110401685	NKD2	-1.280529982
PRMT5	-1.110228976	RBFOX3	-1.280326165
NUDCD3	-1.110181528	AIDA	-1.280056233
SPTLC1	-1.109882016	RPS5	-1.279801141
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NSA2	-1.108398885	THUMPD2	-1.278957779
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CFHR4	-1.107841871	CLCF1	-1.278317998
ATG5	-1.106912764	BLOC1S3	-1.278020097
SRCAP	-1.106872561	C14orf102	-1.277830268
HAUS1	-1.10619977	SHC2	-1.277777602
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ATR	-1.105837161	FBXO22	-1.277239442
AHSA2	-1.105334266	SCTR	-1.276928082
EIF3E	-1.104727511	POLR1B	-1.274172151
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UBLCP1	-1.104115654	TRAF3IP1	-1.271830307
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RPLP2	-1.102899636	BUD31	-1.271033674
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CKAP2	-1.100557384	EIF1	-1.269589844
TAF5	-1.100398036	SLC11A1	-1.268889719
SRSF1	-1.100306853	CHD4	-1.268686586
FBXW11	-1.100215742	RPS9	-1.268593949
VPS28	-1.099537324	SPATA6	-1.268105502
PGM5	-1.099134342	PI4K2B	-1.267829829
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NUPL1	-1.09900294	MMGT1	-1.266883109
PMPCB	-1.098865487	LILRA3	-1.266264471
UFM1	-1.098637778	OR5C1	-1.265249631
PHB2	-1.098532471	RBBP4	-1.264947428
HMGCR	-1.09752676	ISM1	-1.264866462
SMG1	-1.097265312	KPNB1	-1.264830663
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DCTN5	-1.096499524	TGM7	-1.264152913
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KIAA0586	-1.095557469	PAPPA	-1.261561488
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IPO11	-1.092724416	ELAC2	-1.260434805
NFYB	-1.091286106	RPL37	-1.260333546
EIF4ENIF1	-1.089089412	MUSK	-1.259842432
C9orf114	-1.08779364	NANOGNB	-1.259692167
LSM11	-1.086214526	SLC6A12	-1.259572819
VRK1	-1.085903324	ATP5I	-1.257875017
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RCL1	-1.08390836	RSPH6A	-1.25582562
CSF3R	-1.083676018	UBR5	-1.254988844
NOP14	-1.083433165	FLT3LG	-1.254392482
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UBA52	-1.081345178	TAZ	-1.252841935
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C10orf2	-1.079750514	METTL24	-1.252115773
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ALG11	-1.076921234	PAF1	-1.249100724
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DEF8	-1.07564974	C14orf182	-1.248906915
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TDGF1	-1.068623975	SLC52A3	-1.241971506
ABCB7	-1.068075668	ARL11	-1.24181862
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PRPF6	-1.066762079	CCDC64B	-1.240671479
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LSG1	-1.066166811	PKD2L1	-1.23962038
RCC1	-1.065960233	ADAM23	-1.239416475
ATP5I	-1.065074601	LCA5L	-1.239150196
SERPINE2	-1.061809596	POLR3H	-1.238997098
EIF5B	-1.061589138	RPIA	-1.238667289
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HCFC1	-1.060512155	UBA3	-1.237905617
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BARD1	-1.05653207	C7orf23	-1.236025047
GS1-211B7.1	-1.055638252	RBBP5	-1.235719984
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C19orf43	-1.055590894	NPFF	-1.234690934
PSMA4	-1.054967252	CUL1	-1.234042029
CDC16	-1.054451543	C2orf84	-1.233967522
SFSWAP	-1.054306701	TRIM4	-1.233856391
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BOD1L1	-1.053227865	CEBPZ	-1.233787188
FPGT	-1.052739242	TRAF4	-1.233764083
G6PD	-1.052583161	PRPF38A	-1.233432633
MBD6	-1.051540404	RP4-725G10.1	-1.233421201
TIRAP	-1.051294407	MCL1	-1.2331853
FLI1	-1.050933914	C11orf52	-1.230877202
KIF11	-1.050846083	SHROOM1	-1.230429373
GINS1	-1.050225728	KDM5A	-1.230174275
ATP5B	-1.049973223	AKR1C2	-1.228724497
GNL2	-1.049765519	PLEKHG4	-1.228060686
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CHMP3	-1.049124508	PIGY	-1.227016347
PWP2	-1.049006238	PYGO2	-1.226863313
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C15orf42	-1.046178886	PLLP	-1.225999885
ZFC3H1	-1.045841485	PDCD7	-1.225947903
CHKA	-1.045756653	HIGD1A	-1.225303705
MAPK10	-1.045274203	VN1R2	-1.224415174
LAMA2	-1.044167976	OR1L3	-1.223408953
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CENPH	-1.039411904	KCTD3	-1.219907579
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EFCAB4A	-1.038199677	PNMA1	-1.217902567
DNAJC17	-1.038010644	PAX4	-1.217814145
ASB11	-1.036929888	PTAR1	-1.217028717
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WARS	-1.027713458	GTF3C2	-1.213167613
TDO2	-1.027643685	SLC43A3	-1.213037935
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TMX2	-1.018594261	TLE4	-1.206517106
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PTPDC1	-1.014494149	MRPS17	-1.205828906
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HEATR7B2	-1.013780521	ADRB3	-1.205153273
STXBP3	-1.013247945	POU6F1	-1.205067176
TOMM22	-1.012558371	ASPDH	-1.204316403
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OVGP1	-1.01054944	MGST1	-1.202845243
SCD	-1.009733678	ALG2	-1.202776548
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SEPHS2	-1.008627614	RHOD	-1.201014791
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CSTL1	-1.005623976	SAYSD1	-1.1987253
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C19orf52	-1.004058784	RPS2	-1.19681493
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GLRA1	-0.992025418	KRT34	-1.189748177
TTC37	-0.991617863	RGS9BP	-1.188853876
FAM98B	-0.991481224	KCTD11	-1.188848339
NAA38	-0.991438467	FARSA	-1.188748461
DHDDS	-0.988691739	PES1	-1.188565898
GTPBP2	-0.988589701	KRTAP19-8	-1.188438649
CLEC2L	-0.987481869	PGP	-1.188016303
ATMIN	-0.98739107	SSH1	-1.18739853
MTRNR2L3	-0.986897737	KRT75	-1.187200015
PEA15	-0.985880842	HIST3H2A	-1.186323206
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POLR2A	-0.985787997	COX7A2	-1.18513762
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METTL23	-0.984552151	SLC7A6	-1.183846881
C11orf58	-0.983361828	ZFHX3	-1.183840398
GABPB2	-0.982871152	ELP3	-1.183438845
MCF2L	-0.982605638	KIF20A	-1.182917249
ERAL1	-0.981807872	C16orf54	-1.181264225
HUWE1	-0.981603706	PACSIN3	-1.181015708
HECTD3	-0.981147627	DYNLL1	-1.180939788
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IMP3	-0.98032947	SORCS2	-1.179876485
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CSNK1D	-0.980279306	ACTA2	-1.179634896
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MYC	-0.976957246	C17orf28	-1.177601279
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GART	-0.975986622	ADIPOR1	-1.17704494
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PDCD7	-0.974538454	C22orf15	-1.175284917
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KRT71	-0.973981095	USP1	-1.174349639
PSIP1	-0.973643021	TRIM68	-1.173558611
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TFB2M	-0.972935954	ZNF513	-1.172789767
RPL29	-0.971958171	C12orf39	-1.172351943
OSGEP	-0.971890991	DDX23	-1.17190298
AGPS	-0.971461161	COQ3	-1.17111272
WDR18	-0.970454648	SUPT6H	-1.17109365
SUGP1	-0.970082497	CHCHD6	-1.170420985
KDM4B	-0.969836749	CTNNBL1	-1.169866122
CCDC86	-0.969745821	TMEM14C	-1.169789864
GTF2H5	-0.969218429	DIABLO	-1.169779046
CAPN9	-0.968995126	SLC2A12	-1.169624174
DCTN6	-0.968546036	ACTL6B	-1.169372636
RNASEH2C	-0.968090028	SHD	-1.168908091
HIST2H3D	-0.967550433	VPS26B	-1.16833126
RPL27	-0.967489478	GGTLC1	-1.168228071
ZNF407	-0.96713655	EVL	-1.168155498
GINS4	-0.966658728	RNF133	-1.16814253
ACSM4	-0.966503553	FAM63B	-1.167835578
SLC7A4	-0.966347303	ATAD3B	-1.167526301
ZBBX	-0.966340595	MFSD5	-1.166900503
OR52E2	-0.965484195	FAM209B	-1.166659981
C15orf41	-0.965187476	SOX3	-1.1660714
GJC1	-0.964735678	FAM183A	-1.165952272
SLC25A5	-0.964460262	RGS10	-1.165285654
HNRNPCL1	-0.962960756	CCDC125	-1.165112361
HNRNPA2B1	-0.961640683	TMEM230	-1.164754052
HELZ	-0.961255936	TM6SF2	-1.164689242
HNRNPD	-0.961148313	PHC3	-1.164345153
SNX22	-0.960965128	ALG8	-1.1636855
ANKLE2	-0.960584879	RPL38	-1.163530585
WDR24	-0.960325608	SMC5	-1.162725855
ATP6V1H	-0.960046498	TECRL	-1.162608446
RPS6	-0.959802418	INSM2	-1.162511608
ARPC2	-0.959198251	ANKFN1	-1.162254029
MRPL27	-0.958820312	HIST3H3	-1.161849667
COA5	-0.95865868	MEGF10	-1.161822231

OR13C5	-0.958613032	ALG10	-1.160699223
PADI4	-0.957924378	DKKL1	-1.160593167
PRPF38A	-0.95763203	MPV17L	-1.160523288
C8orf82	-0.957027162	SS18L2	-1.160401447
TOP2A	-0.956991206	TMEM120B	-1.160003583
USP39	-0.954340951	TMEM109	-1.159426773
WDR70	-0.952987464	OR52H1	-1.159077488
BRCA2	-0.952182964	PLA2G2E	-1.158794855
MCM2	-0.951805581	ANKMY2	-1.158296055
IER5	-0.951797441	FOXD4L1	-1.158115705
AHSA1	-0.951408637	SH2D3A	-1.157904008
GEMIN7	-0.951372303	CRTAP	-1.157674178
EED	-0.950724816	MARCKS	-1.15760582
SMAD4	-0.950573159	DDX46	-1.157570195
MESDC2	-0.950053433	RPL13	-1.157504332
SLC22A25	-0.949922009	FAM216B	-1.157183413
NSMCE1	-0.949292453	PPP4R2	-1.157119162
BAP1	-0.948836345	TSPAN16	-1.157094764
TMEM237	-0.948441404	UTP6	-1.156869212
NEU3	-0.948069192	PI3	-1.156510368
TEN1	-0.94697411	BRSK1	-1.155649364
SYS1	-0.946634416	TNNC2	-1.15556236
TMED10	-0.946277895	CCDC19	-1.155391718
KLF4	-0.946216742	FLYWCH2	-1.155383306
S100A10	-0.94576215	PTCH1	-1.155025182
C11orf57	-0.945597045	SHISA7	-1.154703726
FAM204A	-0.945399507	KDM4C	-1.154270933
UBL5	-0.945324581	ARHGAP36	-1.15423169
METTL16	-0.945208816	YDJC	-1.154229712
GTF3C1	-0.945069331	SPTLC1	-1.154192067
ASNS	-0.944760908	HMHB1	-1.153717498
PKMYT1	-0.94465765	TNNT3	-1.153541832
MRPL44	-0.943978471	TTC27	-1.15316121
NUP35	-0.943646315	IL6R	-1.153125602
PPYR1	-0.943328666	SYVN1	-1.152995283
SMG5	-0.942586637	CTNNBIP1	-1.152695365
RNF217	-0.941885759	CRLF3	-1.152200608
CPSF4	-0.941442272	SYCE2	-1.152198016
AKAP10	-0.940566385	KIF12	-1.152077246
WEE1	-0.939097678	GEMIN4	-1.151734538
C3orf77	-0.937721113	USP54	-1.151450973
LGALS9C	-0.937476407	RNPEP	-1.151140802
SUZ12	-0.937098269	CATSPER1	-1.151075373
PSMA7	-0.936080385	LYSMD4	-1.150886339
ALDOA	-0.935866715	PLOD1	-1.150877531
PAK1IP1	-0.935775537	SHROOM2	-1.150659978
SYMPK	-0.935542469	C2orf69	-1.150544498
GNL3L	-0.935536653	SYCN	-1.150379088
TXNDC9	-0.935104271	PABPN1	-1.150224404
UBE3D	-0.935012347	TARS	-1.149025971
GLYCTK	-0.93464153	NUPL1	-1.148997097
SLC3A2	-0.934296036	MAN2B2	-1.148385262
TAF7L	-0.933546227	CRYAA	-1.148277098
SMS	-0.933386778	NDST2	-1.147847842
SAFB	-0.933374052	MRPL36	-1.14754419
RP11-466G1	-0.932142451	OAS2	-1.147355516
MLKL	-0.931947868	KRT20	-1.147237746
C18orf21	-0.931878495	RAX	-1.146544905
CENPA	-0.931850229	MED22	-1.14647268
SMARCB1	-0.931804265	PCDHB8	-1.146301319
RIOK1	-0.931217515	EXOSC5	-1.146019271
POP5	-0.930830015	MTHFD2	-1.145860082
SCAF11	-0.930571845	TMPRSS11BNL	-1.145855673
SLC44A2	-0.930391388	THBD	-1.145684107
GRWD1	-0.930200191	TCOF1	-1.145635716
DMAP1	-0.929531228	LCP2	-1.14563327
VRTN	-0.929439281	DDX5	-1.145354266
NARFL	-0.929338565	CFI	-1.145305361
RNF135	-0.928162601	SERAC1	-1.145252469
SPC24	-0.928075601	KCTD8	-1.145044577
FAM63B	-0.927739551	HCFC1	-1.143604518

Table S5 | Output of the RIGER algorithm for the inital A375 PLX screen comparing PLX (mean of the two replicates at day 14) to DMSO control (mean of the two replicates at day 14). The weighted sum method was used to convert sgRNAs to genes. Genes are sorted by RIGER rank.

Gene	# Hairpins	NES	Gene rank	p-value	p-value rank
NF2	4	0.0007519	1	0.000004	2
MED12	4	0.001131	2	0.000004	3
CUL3	6	0.001218	3	0.000006	5
CLDN10	4	0.001504	4	0.000005	4
NF1	2	0.001812	5	0.000001	1
TADA1	4	0.003295	6	0.000035	6
TADA2B	3	0.004823	7	0.000046	7
SPECC1	9	0.005485	8	0.000146	11
CCDC101	3	0.006606	9	0.000082	8
ALG3	4	0.006728	10	0.000118	9
P4HB	3	0.009702	11	0.000189	12
EED	4	0.0106	12	0.000313	15
TAF6L	3	0.01063	13	0.000234	13
MED15	4	0.01175	14	0.000382	17
NPPC	6	0.01229	15	0.000575	24
TAF5L	2	0.01247	16	0.000141	10
PGD	3	0.013	17	0.000349	16
LGALS4	4	0.01351	18	0.00051	22
TAOK1	3	0.01431	19	0.000429	19
CD320	6	0.01431	20	0.000824	30
CCNC	5	0.01475	21	0.000735	25
SMARCB1	3	0.01552	22	0.000501	21
ASIC1	6	0.0162	23	0.001042	34
MED19	4	0.01662	24	0.000754	27
GADD45GIP1	4	0.01713	25	0.000795	29
MED23	2	0.01827	26	0.000301	14
ZDHHC15	4	0.01909	27	0.000988	33
TWF2	6	0.01926	28	0.001489	41
ADRA2B	3	0.02072	29	0.000873	31
PDC	6	0.02089	30	0.001707	50
KCTD10	3	0.02106	31	0.000896	32
MFSD9	2	0.0211	32	0.000419	18
TXNDC17	4	0.02167	33	0.00128	38
MED16	4	0.02186	34	0.001299	40
TADA3	2	0.02199	35	0.000455	20
PDCD10	5	0.02261	36	0.001744	51
TNFRSF17	4	0.02341	37	0.001491	42
DARS	6	0.02349	38	0.002111	61
ELMOD1	2	0.0235	39	0.000523	23
ARID1A	4	0.02355	40	0.001505	43
GNB2L1	4	0.02396	41	0.001556	44
SCPEP1	4	0.02439	42	0.001613	45
KEAP1	4	0.02458	43	0.001632	47
NCOR2	4	0.02481	44	0.00166	48
OR2T33	3	0.02498	45	0.001231	37
BCL2L12	4	0.02546	46	0.001761	53
SPOPL	3	0.0256	47	0.001289	39
FGGY	6	0.0256	48	0.002495	68
CA7	6	0.02599	49	0.002567	69
JMJD4	6	0.02614	50	0.002601	70
MYO9B	4	0.02679	51	0.001952	57
FAM19A4	6	0.02705	52	0.002769	76
EBF4	4	0.02722	53	0.002002	59
TTC4	5	0.02815	54	0.002705	74
DPH2	6	0.02815	55	0.00298	82
DRAP1	4	0.02815	56	0.002136	62
C1orf49	7	0.02818	57	0.003353	87
ATXN2L	2	0.02843	58	0.000746	26
CCT8	2	0.02869	59	0.000757	28
INA	4	0.0287	60	0.00224	64
SPRED1	3	0.02928	61	0.001682	49
FAM205A	3	0.02985	62	0.001761	52
ZNF679	4	0.02985	63	0.002404	66
RARRES1	5	0.03018	64	0.003121	86
OXR1	12	0.03056	65	0.004951	111
ABCB5	9	0.03079	66	0.004499	103

PCIF1	3	0.03083	67	0.00186	54
TSPAN1	4	0.03109	68	0.002605	71
GEN1	4	0.03128	69	0.002637	72
EIF3D	4	0.03135	70	0.00265	73
CD4	4	0.0317	71	0.002719	75
RASGEF1C	3	0.03173	72	0.001958	58
RFX4	8	0.03174	73	0.004515	104
EP300	4	0.03223	74	0.002802	77
MMS19	4	0.0323	75	0.002818	78
HEBP1	4	0.03287	76	0.002925	80
DOK2	3	0.03288	77	0.00211	60
BRD9	7	0.03336	78	0.004695	109
MAP1LC3A	3	0.03376	79	0.002217	63
GPR123	2	0.0343	80	0.001072	35
FH	6	0.03453	81	0.004382	102
NUGGC	3	0.03519	82	0.002409	67
OR52E2	2	0.03523	83	0.001141	36
CRNN	6	0.03558	84	0.004655	107
HDAC6	4	0.03565	85	0.003451	88
AHCYL2	6	0.03793	86	0.005333	117
ZC3H18	3	0.03821	87	0.002841	79
RGS2	5	0.0384	88	0.005052	113
TMED3	3	0.03892	89	0.00293	81
TXNIP	5	0.03944	90	0.005299	116
MLN	3	0.03958	91	0.003008	83
CLEC2B	3	0.03965	92	0.003019	84
CASQ2	3	0.03991	93	0.003063	85
GMDS	6	0.04171	94	0.006445	141
UBE2M	2	0.0418	95	0.001626	46
RNF7	5	0.0423	96	0.006005	129
CRYGN	3	0.04249	97	0.003478	89
NDUFA8	3	0.04313	98	0.003571	90
NCL	5	0.04333	99	0.006281	133
PLK4	5	0.04346	100	0.006321	134

Table S6 | Output of the RIGER algorithm for the transduction replicate A375 PLX screen comparing PLX (mean of the two replicates at day 14) to DMSO control (mean of the two replicates at day 14). The weighted sum method was used to convert sgRNAs to genes. Genes are sorted by RIGER rank.

Gene	# Hairpins	NES	Gene rank	p-value	p-value rank
MED12	4	0.00051	1	0.000002	1
CUL3	6	0.0008262	2	0.000002	2
NF2	4	0.001589	3	0.000005	3
TADA1	4	0.00185	4	0.000007	4
TADA2B	3	0.00213	5	0.00001	5
RBL1	3	0.004575	6	0.000041	6
TAF6L	3	0.006689	7	0.000085	8
OR8S1	4	0.008042	8	0.000157	10
MED23	2	0.009179	9	0.000081	7
SLC41A3	4	0.009526	10	0.000244	14
CCDC101	3	0.01002	11	0.000201	11
LCOR	4	0.01057	12	0.00031	17
GPR98	3	0.01074	13	0.000239	13
KCNA2	8	0.01187	14	0.000666	27
MED15	4	0.01231	15	0.000416	18
MT1F	2	0.01255	16	0.000141	9
MYL7	4	0.01261	17	0.000445	20
SLC7A11	5	0.01288	18	0.000554	23
MTRF1	3	0.0145	19	0.000445	19
ELF1	3	0.01465	20	0.000454	21
METAP1D	4	0.01479	21	0.000612	25
FAM160A2	4	0.01497	22	0.000623	26
TAF5L	2	0.0154	23	0.000207	12
NF1	2	0.01711	24	0.000261	15
DSEL	2	0.01782	25	0.000287	16
RAP1GAP2	4	0.01915	26	0.000992	29
MPG	6	0.0197	27	0.001548	41
MED16	4	0.02023	28	0.001103	31
XKR4	4	0.02069	29	0.001163	32
ERP27	4	0.02156	30	0.001269	35
MAB21L2	3	0.02162	31	0.000938	28
ASIC5	5	0.02172	32	0.001596	42
MSMB	5	0.02184	33	0.001613	43
ZNF182	4	0.02211	34	0.001328	37
ZNF345	2	0.02256	35	0.000479	22
TNFSF18	4	0.02276	36	0.00141	39
NDUFAF2	3	0.02312	37	0.001063	30
PDCD10	5	0.02319	38	0.001844	49
CCNC	5	0.02425	39	0.002022	52
SPRED1	3	0.02451	40	0.001188	33
GDPD2	6	0.02456	41	0.002293	57
DYRK3	4	0.02457	42	0.001629	44
MBP	9	0.02489	43	0.002965	71
PARP3	3	0.02518	44	0.001243	34
UBE2M	2	0.02542	45	0.000595	24
HDGF	3	0.02545	46	0.00127	36
KCNC2	7	0.02554	47	0.002731	66
GALNS	4	0.02604	48	0.00184	47
METTL21B	4	0.02605	49	0.001842	48
BTBD17	3	0.02641	50	0.001371	38
HSD11B1	5	0.02689	51	0.002482	61
LGR5	4	0.02892	52	0.002269	56
BUB1B	4	0.02924	53	0.0023	58
MRFAP1L1	3	0.02926	54	0.00168	45
CCDC83	4	0.02932	55	0.002316	59
DRAP1	4	0.02937	56	0.002321	60
RELT	3	0.02984	57	0.001756	46
RANBP9	3	0.0307	58	0.001849	50
HMMR	4	0.03099	59	0.002589	64
MALSU1	3	0.03115	60	0.001886	51
TACC1	6	0.03181	61	0.003733	94
HOXC13	4	0.03205	62	0.00277	67
EAPP	4	0.03259	63	0.002875	68
C1QA	6	0.03263	64	0.003918	99
SELRC1	3	0.03276	65	0.00209	53
B3GALNT2	6	0.03279	66	0.003962	101

RBM15B	3	0.03299	67	0.002127	54
PDE12	6	0.03326	68	0.004098	104
PAFAH2	6	0.03339	69	0.004132	106
LAMA3	8	0.03369	70	0.005071	132
TDRD5	6	0.03397	71	0.004252	108
MBNL2	4	0.03435	72	0.003193	76
ADI1	6	0.03487	73	0.004464	111
MED19	4	0.03523	74	0.003361	81
PRKRA	5	0.03524	75	0.004253	109
ATP1B4	4	0.03532	76	0.003379	83
PRR7	4	0.03545	77	0.003414	84
GBP2	6	0.03557	78	0.004654	116
KCTD15	4	0.03616	79	0.003546	87
MAPKAPK3	4	0.03631	80	0.003576	89
MRPS12	3	0.0364	81	0.002585	63
TNR	6	0.03661	82	0.004941	127
PET117	3	0.03666	83	0.002611	65
SRM	5	0.03672	84	0.004589	114
INO80E	4	0.03707	85	0.003727	93
ZSWIM6	4	0.0372	86	0.003755	95
SLC4A3	6	0.03732	87	0.005147	134
CDKL4	4	0.03795	88	0.003903	98
EED	4	0.03863	89	0.004041	103
MRPL17	3	0.03885	90	0.002918	69
ANGEL2	5	0.03886	91	0.005154	135
PLK1	4	0.03896	92	0.00412	105
CARS2	3	0.03954	93	0.003005	72
PODN	6	0.03971	94	0.005858	150
AMPD2	6	0.03997	95	0.005936	151
TRIM67	2	0.04032	96	0.001521	40
ACOX1	3	0.04046	97	0.003153	74
PRPF4B	3	0.04046	98	0.003153	75
TCEB2	4	0.04073	99	0.004475	112
VAX1	5	0.04079	100	0.005648	147

Table S7 | Comparison of the top 20 hits between the two A375 PLX infection replicate screens by RIGER rank. RNAi gene enrichment ranking (RIGER) uses a two-sample weighted likelihood ratio test to measure the support for a gene using the enrichment of the sgRNAs (or shRNAs) for each gene.

1st infection			2nd infection		
Gene symbol	RIGER rank	RIGER *p* value	Gene symbol	RIGER rank	RIGER *p* value
NF2	1	0.000004	MED12	1	0.000002
MED12	2	0.000004	CUL3	2	0.000002
CUL3	3	0.000006	NF2	3	0.000005
CLDN10	4	0.000005	TADA1	4	0.000007
NF1	5	0.000001	TADA2B	5	0.00001
TADA1	6	0.000035	RBL1	6	0.000041
TADA2B	7	0.000046	TAF6L	7	0.000085
SPECC1	8	0.000146	OR8S1	8	0.000157
CCDC101	9	0.000082	MED23	9	0.000081
ALG3	10	0.000118	SLC41A3	10	0.000244
P4HB	11	0.000189	CCDC101	11	0.000201
EED	12	0.000313	LCOR	12	0.00031
TAF6L	13	0.000234	GPR98	13	0.000239
MED15	14	0.000382	KCNA2	14	0.000666
NPPC	15	0.000575	MED15	15	0.000416
TAF5L	16	0.000141	MT1F	16	0.000141
PGD	17	0.000349	MYL7	17	0.000445
LGALS4	18	0.00051	SLC7A11	18	0.000554
TAOK1	19	0.000429	MTRF1	19	0.000445
CD320	20	0.000824	ELF1	20	0.000454

appears in the 20 top of other replicate infection

appears in the 100 top of other replicate infection

Table S8 | Comparison of the top 20 hits between the two A375 PLX infection replicate screens by RSA rank. Redundant siRNA activity (RSA) uses an enrichment cutoff and hypergeometric test to measure the support for a gene using the enrichment of the sgRNAs (or shRNAs) for each gene.

1st infection			2nd infection		
Gene symbol	RSA rank	RSA log *p* value	Gene symbol	RSA rank	RSA log *p* value
MED12	1	-12.467	MED12	1	-11.954
NF2	2	-9.147	NF2	2	-8.766
CUL3	3	-8.578	CUL3	3	-8.174
MED15	4	-7.684	TADA2B	4	-6.512
TADA2B	5	-7.418	CCDC101	5	-6.319
RBL1	6	-6.316	DPH2	6	-6.141
TADA1	7	-5.815	MED15	7	-5.609
CCNC	8	-5.483	NF1	8	-5.418
CCDC101	9	-5.313	CLDN10	9	-5.174
PDCD10	10	-5.278	PGD	10	-4.944
NOTCH2NL	11	-4.988	TADA1	11	-4.909
PCLO	12	-4.971	ZEB2	12	-4.892
PPP1R8	13	-4.947	CCNC	13	-4.697
C1QA	14	-4.667	TAF6L	14	-4.402
DR1	15	-4.311	SMARCB1	15	-4.371
KCTD10	16	-4.284	BCL2L12	16	-4.228
PDE12	17	-4.236	PDCD10	17	-4.16
SLC25A17	18	-4.209	GADD45GIP1	18	-4.107
BRD9	19	-4.206	ZNF592	19	-4.037
PET117	20	-4.168	ACTA2	20	-4.033

appears in the 20 top of other replicate infection

appears in the 100 top of other replicate infection

Table S9 | Cas9-sgRNA array screening constructs used. Names and targeting sequence for all Cas9-sgRNA constructs used for validation in A375 screen. Cas9-sgRNAs with *names in italics* are contained in the GeCKO library.

Name	**sgRNA 20bp sequence**
NF2_sg1	AAACATCTCGTACAGTGACA
NF2_sg2	ATTCCACGGGAAGGAGATCT
NF2_sg3	CCTGGCTTCTTACGCCGTCC
NF2_sg4	GTACTGCAGTCCAAAGAACC
NF2_sg5	CACAGTGGCCTGGCTCAAAA
MED12_sg1	AGGATTGAAGCTGACGTTCT
MED12_sg2	CGTCAGCTTCAATCCTGCCA
MED12_sg3	CTCAGAGATTGCTGCATAGT
MED12_sg4	ACAGGTCATCTTAATGAGCC
MED12_sg5	GGGGCTGTGGTTCCACGATA
NF1_sg1	GTTGTGCTCAGTACTGACTT
NF1_sg2	ACACTGGAAAAATGTCTTGC
NF1_sg3	AGTCAGTACTGAGCACAACA
CUL3_sg1	CTTACCTGGATATAGTCAAC
CUL3_sg2	GAATCCTGTTGACTATATCC
CUL3_sg3	GACCTAAAATCATTAACATC
CUL3_sg4	TGCCAGATGTTAATGATTTT
CUL3_sg5	TTATTTAGTCGTGTGCCAAA
TADA1_sg1	ACTGGGCTAACCTAAAGCTG
TADA1_sg2	TCTGCTTGAACCACAGCTTT
TADA1_sg3	GGAGGAAATCATTGTGAGAA
TADA1_sg4	TCTTTAGTGCAATCAGAATC
TADA2B_sg1	ACGGCGGGCGCTTCACGCTC
TADA2B_sg2	GCCATCGAGCAGTTCGGCTT
TADA2B_sg3	GCACCTTCTCGCGATCTGAC
TADA2B_sg4	GCTCCTGTCAGATCGCGAGA
Control_sg1 (EGFP_sg5)	GAAGTTCGAGGGCGACACCC
Control_sg2 (EGFP_sg6)	GGTGAACCGCATCGAGCTGA

Table S10 | shRNA array screening constructs used. Names and The RNAi Consortium (TRC) identification numbers for all shRNA constructs used for validation in A375 screen.

Name	TRC ID	Targeting Sequence
NF2_sh1	TRCN0000010397	GAAGCAACCCAAGACGTTCAC
NF2_sh2	TRCN0000018338	TAGTTCTCTGACCTGAGTCTT
NF2_sh3	TRCN0000039974	GCTCTGGATATTCTGCACAAT
NF2_sh4	TRCN0000039975	GCTTCGTGTTAATAAGCTGAT
MED12_sh1	TRCN0000018574	GCAGCATTATTGCAGAGAAAT
MED12_sh2	TRCN0000018575	GCTGTTCTCAAGGCTGTGTTT
MED12_sh3	TRCN0000018576	CGGGTACTTCATACTTTGGAA
MED12_sh4	TRCN0000018578	GCAGAGAAATTACGTTGTAAT
NF1_sh1	TRCN0000039714	GCCAACCTTAACCTTTCTAAT
NF1_sh2	TRCN0000039715	CCTCACAACAACCAACACTTT
NF1_sh3	TRCN0000039716	CCTGACACTTACAACAGTCAA
NF1_sh4	TRCN0000039717	GCTGGCAGTTTCAAACGTAAT
TADA2B_sh1	TRCN0000237951	CGTGACTGTGAAGACTATTAT
TADA2B_sh2	TRCN0000237949	ATGATTACGAGATCGAGTATG
TADA2B_sh3	TRCN0000237950	ACATCGCCCGTGACTACAATC
NullT_1	TRCN0000208001	n/a
NullT_2	TRCN0000231782	n/a

Supplementary References and Notes

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