## CENP-A associated IncRNAs influence chromosome segregation in human cells

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#### Abstract

Transcription occurs ubiquitously throughout non-coding parts of the genome, including at repetitive $\alpha$-satellite DNA elements which comprise the majority of human centromeres. The function of temporally regulated centromeric transcription, and transcripts, is consequently a topic of intense investigation. In this study, we use high throughput approaches to identify and describe lncRNAs associated with the centromere specific histone variant CENP-A that arise from the transcription of specific centromeres at early G1, which we then show are physically associated with centromeres, and which are functionally necessary for accurate chromosome segregation. Targeted depletion of one such centromeric RNA, which originates from a single centromere, is sufficient to increase the frequency of chromosome segregation defects. These data support the emerging paradigm of the necessity of centromere-specific lncRNAs in the integrity of faithful chromosome segregation.


## INTRODUCTION

Centromeres are specialized chromosomal domains essential for kinetochore formation and attachment of the microtubule spindle, and consequently required for faithful chromosome segregation during cell division (1). The integrity of this chromatin region is maintained by a unique epigenetic landscape that is defined by the centromeric histone variant CENP-A, histone post-translational modifications, DNA methylation, chromatin-binding kinetochore proteins, and non-coding RNAs (2,3). Indeed, despite the lack of known genes in most centromeres, centromeric transcription is ubiquitous across eukaryotic species (4-19). In many of the species studied, the repetitive sequence of centromeres has contributed to the challenge in characterizing centromere-derived long non coding RNAs (lncRNAs). In humans, centromeric DNA consists of 171 bp monomer $\alpha$-satellite repeats (20). Arranged in a tandem fashion, these AT-rich repeats lack genes and share $40-100 \%$ sequence identity across different chromosome
centromeres (21). The organization of monomeric or dimeric units of this base sequence into higher order repeats (HOR) can serve to distinguish individual centromeres (22). Recent work has demonstrated that lncRNAs are transcribed during late mitosis - early G1 by RNA polymerase II (RNAPII) from centromeric human $\alpha$-satellite DNA, where they interact with the essential inner kinetochore proteins CENP-A and CENP-C $(8,12,19)$. Excitingly, this phenomenon appears to be evolutionarily conserved across humans, Drosophila and Xenopus $(17,18)$. In mammals, overexpression or down-regulation of centromeric $\alpha$-satellite RNAs is associated with errors of chromosome segregation arising from centromeric defects during mitosis (10-12,19,23). Finally, a recent study in Drosophila confirms the importance of centromere transcription-assisted loading of CENP-A via factors such as FACT and Mis18 (24). The accumulation of evidence from multiple organisms synthesized into a working hypothesis suggests that centromeric transcripts and transcription are both essential for the accurate spatial and temporal targeting of centromeric proteins at the centromere, and consequently, contribute to accurate segregation of chromosomes during mitosis. Several outstanding questions remain to be answered: whether all centromeres in a given set of chromosomes are uniformly transcribed; the identity of these transcripts; whether centromeric transcripts have a discrete length reflecting a defined transcriptional unit; whether they bind in cis or in trans across different centromeres in a genome; the consequences of their loss or over-abundance; and finally, the mechanism by which cenRNAs might bind kinetochore proteins directly. In this study, we report our progress in investigating five out of these six important questions.

In our previous study (19), we reported that in early G1, RNAPII transcribes human centromeres, generating $\sim 1.3 \mathrm{~kb}$ long non-coding centromeric RNAs (cenRNAs) which are associated with soluble pre-assembly CENP-A/H4/HJURP- and CENP-A- chromatin-complexes. Depletion of these transcripts using $\alpha$-satellite consensus sequence shRNAs leads to defective CENP-A loading in early G1 at a subset of centromeric fibers, resulting in chromosome mis-segregation and other cellular defects. These data, along with work of others cited above, strongly suggested a role for cenRNAs in maintaining the integrity of centromeric chromatin and cell division. In this study, to better characterize centromeric RNAs and their function, we performed soluble and chromatin bound CENPA associated RIP-seq (RNA-immunoprecipitation coupled to high throughput sequencing) from HeLa cells at early G1. Using this strategy, we identify several hundred cenRNAs which map to individual chromosomal centromeres, with strong homology to known centromeric $\alpha$-satellite repeats, and which range from 300-2500 bases in length. Focusing our efforts on a subset of these cenRNAs, we show that one cenRNA, approximately $\sim 1 \mathrm{~kb}$ long, transcribes uniquely from chromosome 17 , co-localizes with centromeric markers, and appears to be poly-adenylated. Functional characterization of this cenRNA by down-regulation of the transcript, demonstrates that its loss increases the frequency of chromosome segregation defects. These data support the emerging paradigm that centromeric RNAs are crucial players in the maintenance of centromeric integrity in higher eukaryotes.

## MATERIAL AND METHODS

## Tissue culture

HeLa cells were grown at $37^{\circ} \mathrm{C}, 5 \% \mathrm{CO}_{2}$, in Dulbecco's modified Eagle's medium high in glucose and

L-glutamine (\#11965; Thermo Fisher Scientific/Gibco, Grand Island, NY) supplemented with 10\% Fetal Bovine Serum (\#26140-079; Thermo Fisher Scientific/Gibco) and 1X Pen/Strep solution (\#10378-016; Thermo Fisher Scientific/Gibco).

Cells were synchronized by double thymidine block ( 0.5 mM , \#T9250; Sigma-Aldrich, Saint Louis, MO). After a first block of 19 hours, cells were released for 9 hours, followed by a second thymidine block of 16 hours. Then, cells were released for the appropriate time ( 10 hours for mitosis and 11 hours for early G1, as described previously in (19)).

## Antibodies

Antibodies are commercially available. Supplemental Table 1 lists all antibodies used for each experiment.

## shRNA

shRNAs incorporated into pGFP-V-RS plasmid vectors were purchased from Origene (Rockville, MD). Supplemental Table 2 lists sequences of these shRNA.

## Primers

Primers were purchased from Integrated DNA Technologies (Coralville, IA). Supplemental Table 3 lists primer sequence used for each experiment.

## BLAST on cenRNA\#1

BLAST was performed on untranslated nucleotide sequence (blastn). Sensitive settings were: word size $=7$ and expect value threshold $=10$, with no low complexity filtering or repeat masking. Multiple blastn runs with variations of these parameters did not yield additional hits. To make our searching results more intuitive to interpret (as opposed to E-values and bit scores), a negative control sequence consisting of random sequence of the same length as cenRNA\#1 (19) and with the same GC percent ( $47.4 \%$, which is close to the human genome average of $46 \%$; (25)) was generated. Random GC matched sequence for control was generated from the random DNA server at UC Riverside (http://www.faculty.ucr.edu/~mmaduro/random.htm; Morris Maduro, accessed on February 2, 2015). The reference sequence of the 17bp CENP-B box (5'-CTTCGTTGGAAACGGGA-3') is from (26). Adapter sequences identified in cenRNA\#1 are described in (27).

## RNA Immuno-Precipitation - sequencing (RIP-seq)

RNAs associated to CENP-A or agarose bead (mock-IP) were purified and identified following the protocol described in (28). Briefly, for each condition, five F175 flasks of HeLa cells at a final confluency of $80 \%$ were used per RIP-seq. Trypsinized cells were washed two times with cold 1X PBS; 0.1\% Tween 20 (\#P2287, Sigma-Aldrich), before fixation with $0.1 \%$ formaldehyde (\#15680, Electron Microscopy Sciences, Hatfield, PA) in 1X PBS. The reaction was stopped by addition of 125 mM glycine ( $\# 50046$, Sigma-Aldrich). Then, nuclei were isolated in TM2 buffer ( 20 mM Tris$\mathrm{HCl}, \mathrm{pH} 8.0$ (\#15568-025, Thermo Fisher Scientific); 2 mM MgCl 2 (\#AM9530G, Thermo Fisher Scientific); 0.5 mM PMSF (\#78830, Sigma-Aldrich); 1X complete protease inhibitor cocktail (\#05892953001, Roche, Indianapolis, IN) complemented with $0.5 \%$ Nonidet ${ }^{\mathrm{TM}} \mathrm{P} 40$ Substitute (NP40, \#74385, Sigma-Aldrich) and 10mM Ribonucleoside Vanadyl Complex (RVC, \#1402, New England Biolabs-NEB, Ipswich, MA), and washed in TM2 buffer complemented with 10 mM RVC. Chromatin was MNase-digested (MNase, \#N3755, Sigma-Aldrich) in 0.1 M TE buffer ( 0.1 M NaCl (\#24740-011, Thermo Fisher Scientific); 10 mM Tris-HCl, pH 8.0; 0.2mM EGTA (\#03777, SigmaAldrich) in presence of $2 \mathrm{mM} \mathrm{CaCl}_{2}(\# 746495$, Sigma-Aldrich). After addition of 10 mM EGTA to stop the MNase action, nuclear pellet was resuspended in 1 mL low-salt buffer ( 0.5 X PBS, 5 mM EGTA, 0.5 mM PMSF, 1 X complete protease inhibitor cocktail) complemented with 50 units of murine RNase inhibitor (\#M0314S, NEB), and chromatin was extracted overnight at $4^{\circ} \mathrm{C}$ in an end-over-end rotator. After centrifugation, the supernatant was precleared with $30 \mu \mathrm{~L}$ of protein A/G Plus agarose beads (\#sc2003,Santa Cruz Biotechnology, Dallas, TX) for 30 min at $4^{\circ} \mathrm{C}$ in an end-over-end rotator, and then, incubated with the anti-CENP-A primary antibody or no antibody for a minimum of 4 hours and a maximum of 12 hours at $4^{\circ} \mathrm{C}$ in an end-over-end rotator. CENP-A/primary antibody complex and mock-IP sample were immunoprecipitated with $50 \mu \mathrm{~L}$ of protein $\mathrm{A} / \mathrm{G}$ plus agarose beads for 2 hours at $4^{\circ} \mathrm{C}$ on the end-over-end rotator. Beads were washed three times with 1 mL low-salt buffer containing murine RNase inhibitor and complete protease inhibitor cocktail. To isolate immuno-precipitated RNA, RNA-protein complex was eluted (elution buffer: $1 \%$ SDS; 0.1 M sodium bicarbonate (\#S6014, Sigma-Aldrich)), denaturated, treated sequentially with proteinase K (\#AM2548, Thermo Fisher Scientific/Ambion) and DNaseI (\#AM2222, Thermo Fisher Scientific/Ambion), and purified by phenol:chloroform:isoamylalcohol method. RNA concentration was determined by measurement on a UV-spectrophotometer and the quality of RNA was verified using a Bioanalyzer (\#5067-1511, Agilent Technologies, Santa Clara, CA).

## RIP-seq library construction and sequencing

To prepare RIP samples for sequencing, libraries were constructed with the Illumina TruSeq ChIP Library Preparation Kit (IP-202-1012 \& IP-202-1024, Illumina, San Diego, CA). RIP libraries were barcoded and run in multiplex on a HiSeq 2500 instrument (Illumina) by the NCI-Sequencing Core Facility. Cluster generation was performed using an Illumina HiSeq PE Cluster Kit v4 cBot (\#PE-4014001, Illumina). The sequencer was run for 125 cycles in paired-end mode. Base calling accuracy was high for each sample, with $>90 \%$ of bases with a quality score of at least Q30 $(99.9 \%$ accuracy in Phred scale). RIP-Seq experiments were performed in duplicate, and included both, input and mockIP samples as negative controls. Raw reads total for each sample ranged from 49 to 112 million reads.

## Computational analysis

To identify putative centromeric transcripts from the RIP-seq results, we followed a computational pipeline as described in our recently published methods book chapter on this topic (28). Briefly, raw reads in fastq format were cropped to remove low quality base calls from read ends with Trimmomatic (29). These pre-processed reads were then used in a first pass alignment to the repeating rDNA subunit (U13369.1, retrieved from GenBank) with Bowtie2 (30) in sensitive mode, to deplete ribosomal transcripts in silico. The unaligned reads from this process were used for further analysis. These reads were mapped to the Build 38 reference genome (hg38) using Tophat v2.1.0 (31). For Tophat alignment, up to three read mismatches (and an edit distance of three) were allowed for alignment, and only a single best alignment was reported for each read (the '-g 1' option). The centromeric sequence included in this version of the reference allowed us to map reads deriving from centromeric transcripts. Transcripts were defined from these alignments by reference-guided transcript assembly using Cufflinks (31). These assemblies were merged and transcript abundances were estimated with Cufflinks. Quantitative tracks for browser visualization were generated using deepTools (32). For visualization, Bowtie2 alignments were run in local mode (which allows soft-clipping), and enrichment relative to input was plotted as the subtraction of the depth normalized coverage in the input sample from the depth normalized coverage in the IP sample.

Open reading frame (ORF) finding was performed using the NCBI Orf Finder tool (https://www.ncbi.nlm.nih.gov/orffinder/), selecting "ATG only" to define ORF start sites. To search for TATA-boxes, we used the "fuzznuc" Emboss package that can map the consensus motif with amibiguity codes ("TATAWAAR"; (33)). For evidence of other gene elements, we used Promoter 2.0 and Genscan on the region $+/-2 \mathrm{~kb}$ from the cenRNAs $(34,35)$.

Motif enrichment was performed with MEME (36). Since this tool limits the amount of sequence that may be input at one time, we separated out transcript sequences into four subsets and ran them individually. The maximum motif size was set to 171 bp , the length of the $\alpha$-satellite monomer. We analyzed the ten highest reported scoring motifs. Sequence logos for the top-scoring motif in each subset is presented in Supplemental Figure 1A. Each of these motifs were highly similar to $\alpha$-satellite monomer ( $88-98 \%$ identical over $98-100 \%$ of the query).

To generate distance trees for the complete set of cenRNAs, we aligned them using MUSCLE (Multiple Sequence Comparison by Log-Expectation; (37)), and calculated a tree based on average distance using percent identity (Supplemental Figure 1B). These calculations were implemented with Jalview (38). The results were then visualized in Dendroscope 3 to make the tree more interpretable (39). Since branching patterns can differ by algorithm, we generated multiple trees for comparison. Representative of this analysis, trees using alternative alignments Clustal and clustering performed with Unweighted Pair Group Method with Arithmetic Mean (UPGMA), including bootstrap results (using Geneious v.10.0.6; (40)), are shown in Supplemental Figure 1C-F. We note that a fraction of transcripts do not cluster at the bootstrap level of $70 \%$ support, but despite this, separation of transcripts into clusters was observed consistently.

## Poly-adenylation of candidate cenRNAs

Total RNAs from HeLa cells were purified with Trizol reagent (\#15596026, Thermo Fisher Scientific/Ambion) following manufacturer instructions. To run out genomic DNA contamination, these total RNAs were incubated with 4 units of DNase I (\#M0303S, NEB) for 30 min at $37^{\circ} \mathrm{C}$. The reaction was stopped by addition of 50mM EDTA (\#351-027-721, Quality Biological, Gaithersburg, MD) and incubated at $75^{\circ} \mathrm{C}$ for 10 min . Then, total RNAs were purified using the Zymo Clean \& Concentratator kit (\#R1015, Zymo Research, Irvine, CA) before being retro-transcribed using SuperScript IV kit (\#18091050, Thermo Fisher Scientific) with either polydT primers or random hexamers following manufacturer instructions. PCR reaction was run using Dream Taq PCR master mix kit (\#K1071, Thermo Fisher Scientific) with $\alpha$-satellite or cenRNA\#4 primers (Supplemental Table 3). Cycling conditions for PCR were: 30 s at $98^{\circ} \mathrm{C} ; 30$ cycles: 5 s at $98^{\circ} \mathrm{C}, 30$ s at $57^{\circ} \mathrm{C}, 20$ s at $72^{\circ} \mathrm{C} ; 300 \mathrm{~s}$ at $72^{\circ} \mathrm{C}$. Finally, PCR products were analyzed on $2 \%$ agarose gel.

## RNA fluorescence in situ hybridization (RNA FISH)

Custom Stellaris RNA FISH probes labeled with Quasar dyes (i.e., Quasar ${ }^{\circledR} 570$ or Quasar ${ }^{\circledR} 670$ ) were designed against specific cenRNAs and purchased from Biosearch Technologies (Petulama, CA). 75\% confluent HeLa cells on poly-L lysine coverslip in 6-well plate were washed three times with HANKS buffer (\#14170112, Thermo Fisher Scientific) and fixed with 4\% paraformaldehyde (\#15714, Electron Microscopy Sciences) in 1X PBS for 10 min at room temperature (RT). After washing cells with 1X PBS two times for 10 min , cells were made permeable in 70\% ethanol (\#61509-0010, Acros Organics, Pittsburgh, PA) overnight at $4^{\circ} \mathrm{C}$. In order to confirm that the observed RNA FISH signal results from the hybridization of the probe with an RNA molecule and not genomic DNA, for every RNA FISH experiment, cells were rinsed once with 1X PBS in presence or absence of $1 \mathrm{mg} / \mathrm{mL}$ of RNase A (\#12091-021, Thermo Fisher Scientific). Cells were pre-incubated with 2X SSC (\#AM9763, Thermo Fisher Scientific/Ambion); 10\% deionized formamide (\#15745, Electron Microscopy Sciences) for 5 min , and incubated with hybridization mix ( $0.1 \mu \mathrm{M}$ RNA FISH probe set diluted in $10 \%$ dextran sulfate (\#S4030, EMD Millipore, Billerica, MA), 2X SSC, $10 \%$ deionized formamide), for 4 hours to overnight at $37^{\circ} \mathrm{C}$ in the dark. Finally, cells were washed twice with $10 \%$ deionized formamide in 2 X SSC for 30 min at $37^{\circ} \mathrm{C}$ and once with 2 X SSC for 5 min at RT. Coverslips were mounted on cells with anti-fade mounting medium Prolong Gold with DAPI (\#P36935, Thermo Fisher Scientific).

## Immuno-fluorescence / RNA FISH (IF/RNA FISH)

IF/RNA FISH experiments were performed as described previously (28). Custom Stellaris RNA FISH probes were purchased at Biosearch Technologies. Briefly, 75\% confluent cells on poly-L lysine coverslip in 6 -well plate were washed three times with HANKS buffer and fixed with $4 \%$ paraformaldehyde in 1X PBS for 10 min at RT. After permeabilization in 0.1\% Triton X-100 (\#T8787,

Sigma-Aldrich) in 1X PBS for 5 min at RT, cells were incubated with anti-CENP-B primary antibody in IF buffer (1X PBS; 1\% normal goat serum (\#005-000-121, Jackson ImmunoResearch, West Grove, PA ); 50 units of murine RNase inhibitor) overnight at $4^{\circ} \mathrm{C}$. After three washes in 1X PBS, cells were incubated with secondary antibody (goat anti-rabbit $\operatorname{IgG}(\mathrm{H}+\mathrm{L})$ secondary antibodies, Alexa Fluor®488 or Alexa Fluor®568 conjugate (Thermo Fisher Scientific) in IF buffer for 1 hour at RT in the dark. To validate the RNA signal, half of slides were treated with 1X PBS complemented with $1 \mathrm{mg} / \mathrm{mL}$ of RNase A. Cells were fixed with $4 \%$ paraformaldehyde in 1X PBS for 10 min , and washed twice with 1X PBS for 10 min . Then, cells were treated for RNA FISH as described earlier in "RNA FISH" section.

## Electroporation of HeLa cells - shRNA depletion of centromeric RNAs

$1.2 \times 10^{6}$ cells were mixed with $100 \mu \mathrm{~L}$ of RT nucleofection reagent (\#VACA-1001, Lonza, Allendale, NJ) and $7 \mu \mathrm{~L}$ of plasmid containing shRNA, or a GFP control to quantify transfection efficiency ( $500 \mathrm{ng} / \mu \mathrm{L}$ of Scrambled, cenRNA\#4A, cenRNA\#4B, $\alpha$-satellite A, $\alpha$-satellite B, H3-GFP). After electroporation with Nucleofector ${ }^{\circledR}$ Device (Lonza, Walkersville, MD) using program O-005 (for high viability), HeLa cells were resuspended in $500 \mu \mathrm{l}$ of warm media. $200 \mu \mathrm{~L}$ of cells were transferred to a 6 -well plate. Two days later, cells were stained for RNA FISH to validate the depletion in cenRNA. Otherwise, they were selected with $0.5 \mu \mathrm{~g} / \mathrm{mL}$ puromycin until day 6 , at which they were fixed and treated for IF.

## Immuno-fluorescence

HeLa cells were grown on poly-D-Lysine-treated coverslips in 6-well plate. After two washes with cold 1X PBS, cells were prefixed for 30 s with cold $4 \%$ paraformaldehyde in PEM ( 80 mM K-PIPES pH6.8; 5 mM EGTA $\mathrm{pH} 7 ; 0,2 \mathrm{mM} \mathrm{MgCl} 2$ ). After washing three times with cold PEM, soluble proteins were extracted for 5 min on ice with $0.5 \%$ Triton X-100 in CSK ( 10 mM K-PIPES pH6.8, 100 mM $\mathrm{NaCl}, 300 \mathrm{mM}$ sucrose, 1 mM EGTA, 3 mM MgCl 2 ). Few drops of $4 \%$ paraformaldehyde in PEM were added for 5 min . Coverslips were then incubated with fresh $4 \%$ paraformaldehyde in PEM for 40 min on ice. After three washes with PEM, cells were permeabilized with $0.5 \%$ Triton X-100 in PEM for 30 min at RT, washed again three times, and blocked in 1X TBS, 3\% Bovine Serum Albumin, 5\% normal goat serum for 1 hour at RT. Finally, cells were incubated with the primary antibody diluted in 1 X TBS, $1 \%$ Bovine Serum Albumin, $5 \%$ normal goat serum overnight at $4^{\circ} \mathrm{C}$ in a humidified chamber. Cells were washed three times for 5 min at RT with 1 X TBS, $0.1 \%$ Tween 20, and incubated with secondary antibody for 1 hour at RT. After washing, coverslips were mounted on slides with antifade mounting medium Prolong Gold with DAPI.

## Microscopy observation and analysis

RNA FISH, IF and IF/RNA FISH slides were observed with a DeltaVision or DeltaVision Elite RT microscopy imaging system (GE Healthcare, Pittsburgh, PA) controlling an interline charge-coupled device camera (Coolsnap, Tucson, AZ) mounted on an inverted microscope (IX-70; Olympus, Center Valley, PA). Images were captured by using a 60 X objective at $0.2 \mu \mathrm{~m}$ z-sections and analyzed with Image J (1.50e; Java 1.6.0_20, NIH, Bethesda, MD).

## Statistical analysis

On each figure is indicated the number of repetition for each experiment (generally $\mathrm{N}=3$ biological replicates; typically, a minimum of 100 cells - $\mathrm{n}=100$ - scored per phenotype measured). Standard error was determined for all quantification measures. To test the significance of chromosome segregation defect measurements, a two-tailed Fisher's exact test was performed. For all tests, $\alpha$ was assumed to be 0.05 . Significant p-values are indicated on the figures or tables with an asterisk each time it was evaluated.

## RESULTS

## Identification of centromeric RNAs by RIP-seq originating from discrete centromeric satellite sequences

To design an unbiased approach to identify potentially repetitive centromeric RNA sequences, we constructed libraries from RIP experiments followed by high-throughput sequencing (RIP-seq), and identified several hundred RNA species associated with CENP-A at centromeres (Figure 1A; (28)). We refined a computational pipeline to assemble putative centromere-derived transcripts from RIPseq reads (Figure 1B; (28)). Briefly, reads deriving from ribosomal transcripts were depleted in silico, mapped to Build 38 reference sequence including centromere sequence models, and assembled into putative transcripts using the Build 38 reference as a guide. This analysis yielded 432 putative transcripts that were at least 300bp in length (the approximate library fragment length), with abundance $\geq 1$ fragment per kilobase per million mapped reads (FPKM) in the chromatin fraction of each of two replicates, and which mapped to centromeres (Figure 1C-F and Supplemental Table 4). The complete set of candidate cenRNAs has a median size of 443bp, and a maximum size of 2450bp (Figure 1G). They were detected on every chromosome except for chromosomes 6, 13, and 14, although low abundance transcript predictions were defined on these chromosomes as well (Figure 1H). Most displayed reduced enrichment in shRNA $\alpha$-satellite samples ( $60-66 \%$ of cenRNAs). These results demonstrate the pervasive nature of centromeric transcription in the HeLa transcriptome, and suggest that centromeric transcripts span a size range from 300-2500 bases, arising from transcripton of a large fraction of centromeres in the human nucleus.

We next searched for recurring motifs in these centromeric RNA sequences using the algorithm MEME. Reassuringly, the top scoring motifs were highly similar to the canonical $\alpha$-satellite monomer (Supplemental Figure 1A), confirming the predominance of $\alpha$-satellite sequence in these transcripts.

To analyze the sequence heterogeneity in our putative cenRNAs, we generated trees computed on percent identity distance (Supplemental Figure 1B-F). Although $\alpha$-satellite sequence is predominant in these transcripts, sufficient differences exist to separate them into four distinct groups, or 'clades.' Although transcripts from the same centromere tended to group together, the branching was not strictly by chromosomal origin. These results demonstrate the diversity of centromeric transcribed sequences, and show that they are separable and identifiable in sequencing experiments. We also assessed whether results from a previous attempt, in which we attempted to clone representative centromeric RNAs using a traditional small RNA cloning strategy (cenRNA\#1) were enriched in this unbiased high throughput RIPSeq data set. We did not detect a previously cloned putative transcript in this dataset. Indeed, after thorough investigation (Supplemental Note 1), we concluded that the contiguous sequence derived from putative cenRNA\#1 cloned by traditional approaches does not represent true centromeric RNA sequences (Supplemental Note 1).

From the RIP-seq centromere-mapping putative transcripts identified above, we selected three candidate cenRNAs for follow-up experiments, based on relative abundance and enrichment relative to controls (cenRNA\#2, cenRNA\#3, cenRNA\#4; Figure 1C-E). Interestingly, each selected cenRNA was also detected in soluble pre-assembly CENP-A RIP-seq, but at less than half the abundance, supporting a relatively stable chromatin association for these targets. A reduction of enrichment was also observed in RIP samples transfected with $\alpha$-satellite shRNA, suggesting these cenRNAs are depleted in our knockdown experiments (8.4-79\% for cenRNA\#2, 24.9-31.2\% for cenRNA\#3, and $9.2-31.7 \%$ for cenRNA\#4; Supplemental Table 4). Each of these transcripts was defined by alignment to centromeric reference assembly, containing sequence in previously described $\alpha$-satellite monomers (20). Using this approach, we observed that cenRNA\#2 maps to chromosome 3 with high sequence similarity to the HOR DSZ1 (41), although RepeatMasker classifies the majority of the transcript region as scaffold attachment region (SAR) class satellite rather than ALR/alpha $(42,43)$. In contrast, cenRNA\#3 and cenRNA\#4 mapped with very high homology to centromeric sequences on chromosome 17 , specifically to the D17Z1 $\alpha$-satellite array $(44,45)$. Thus, these results show the existence of multiple centromeric long non-coding RNAs originating from several chromosomes. In addition, multiple RNAs can be transcribed from one chromosome. We interpret these data to indicate two points. First, that individual centromeres from different chromosomes are competent for transcription, and second, that transcription likely does not have a distinctive single start site per centromere.

We analyzed the sequence characteristics of the cenRNAs for evidence of coding potential. None of them included an open-reading frame (ORF) with 100 or more codons (a commonly used cut-off for defining a $\operatorname{lncRNA} ;(46)$ ). We also searched for protein alignments to six-frame translated cenRNA sequence. Neither cenRNA had evident similarity to human protein, with best hits all from predicted microbial protein sequence (Supplemental Datafile 1). This analysis supports the commonly accepted notion that centromeric transcripts are non-coding.

## Centromeric RNAs are present at discrete centromeric loci in the nucleus during late mitosisearly G1

We, and others, have previously shown that human centromeres are preferentially transcribed by RNAPII at late mitosis - early G1 $(8,19)$. To assess the abundance of expression of these newlyidentified cenRNAs in human cells at early G1, we synchronized HeLa cells to that specific time of the cell cycle and performed RNA FISH. Then, we measured the frequency of cells expressing these cenRNAs by counting cells with a bright RNA FISH focus consistent with known appearance of transcriptionally active foci.

For RNA FISH localization controls, we chose MALAT1 and NEAT1, two well described nuclear lncRNAs, which are ubiquitously expressed in human cells (47). MALAT1 was highly expressed with punctated spots all over the nucleus, whereas NEAT1 signal was more discrete with an average of 7 spots per cell (Figure 2A). This distribution is consistent with the localization of MALAT1 and NEAT1 described in the literature (47), implicating our approach conserve the spatial localization of lncRNAs. Both MALAT1 and NEAT1 were expressed in more than $80 \%$ of late mitosis - early G1 synchronized cells (Figure 2B). To exclude an unspecific hybridization of the RNA probes to genomic DNA, cells were treated with RNase A. As expected, the RNA FISH signal was diminished substantially after RNase A treatment, confirming the the ribonucleic nature of the observed signal and validating the method (Supplemental Figure 2).

Next, we studied the localization of centromeric $\alpha$-satellite RNAs (Figure 2). Consensus centromeric transcripts were revealed by probes designed against the consensus sequence of $\alpha$-satellite repeats derived from (20). On average, seven discrete nuclear spots were observed in $34 \%$ of late mitosis early G1 synchronized cells, but none in cells treated with RNase A (Figure 2B and Supplemental Figure 2). This result suggests that several centromeric RNAs are transcribed from multiple centromeres and are localized in multiple nuclear localizations at the end of mitosis.

Next, we analyzed the localization of the three selected cenRNAs, namely cenRNA\#2, cenRNA\#3 and cenRNA\#4 (Figure 1) using the same approach. Using probes designed against cenRNA\#2, we observed RNA FISH signals were diffuse and similar to background and the RNase A-treated control, suggesting these probes were prone to non-specific recognition of other RNAs in the genome (Figure 2A and Supplemental Figure 2). In contrast, RNA FISH experiments performed with RNA probes designed against cenRNA\#3 and cenRNA\#4 expressed well defined and unique foci in synchronized HeLa cells (Figure 2A). cenRNA\#3 and cenRNA\#4 were observed in $\sim 28 \%$ and $\sim 37 \%$ of late mitosis - early G1 synchronized cells, respectively (Figure 2B). These signals were lost upon RNase A treatment, confirming the ribonucleic nature of the analyzed foci (Supplemental Figure 2).

Next, we characterized these transcripts by determining the chromatin domain to which they are localized. For this purpose, we performed a co-IF/RNA FISH to observe their relative localization to centromeres, using CENP-B, which marks centromeric DNA (Figure 3A). Since these RNAs were originally identified by CENP-A-chromatin RIP-seq (Figure 1), we expected to observe a colocalization or partial co-localization of cenRNAs with CENP-B domains. Reassuringly, in cells expressing centromeric $\alpha$-satellite transcripts, $\sim 74 \%$ of them displayed overlap between CENP-B and $\alpha$-satellite RNA signals (Figure 3B). The absence of RNA FISH signal after RNase A treatment
confirm that the observed $\alpha$-satellite foci were indeed centromeric transcripts and not genomic sequence (Figure 3B). Next, we assessed the relative localization of cenRNA\#4 to centromeres by repeating this co-IF/RNA FISH experiment (Figure 3C). As observed for $\alpha$-satellite transcripts, cenRNA\#4 was also found overlapping with CENP-B signal in $\sim 70 \%$ of cells expressing cenRNA\#4 (Figure 3C). Upon RNase A treatment, the RNA signal was lost (Figure 3C). Thus, our results indicate that in late mitosis - early G1 cells, cenRNA\#4 and $\alpha$-satellite transcripts localize adjacent to CENP$B$ domains.

## Centromeric transcripts are poly-adenylated

Since centromeric RNAs have been reported to be polyadenylated in Drosophila (18), we were curious whether human centromeric transcripts might also contain a poly(A) tail. To test this hypothesis, we retro-transcribed DNase I-treated total human RNAs with either poly(dT) or random hexamer primers, amplified cDNAs and compared profiles of PCR products on agarose gel (Supplemental Figure 3). Using primers designed against centromeric consensus sequence ( $\alpha$-satellite), we observed discrete bands every $\sim 170$ bases (from 170 to 680 bases) after retro-transcription with both poly(dT) or random hexamer primers (Supplemental Figure 3A). These data suggest that these centromeric transcripts are likely polyadenylated. To confirm the ribonucleic nature of the analyzed molecules, several controls were performed. To prove the absence of contaminant in our reaction mix, the experiment was performed without total human RNAs (-RT in Supplemental Figure 3A). We did not observe PCR products in this condition. We also tested the property of primers to self-anneal or dimerize by running a PCR reaction without cDNA (-cDNA in Supplemental Figure 3A). No PCR products were amplified. Altogether, these data suggest that centromeric RNAs are polyadenylated. We decided to further test this hypothesis that cenRNAs present a poly(A) tail by repeating the experiment with primer sets designed against cenRNA\#4 (Supplemental Figure 3B).Similarly to centromeric $\alpha$-satellite transcripts, several discrete bands were observed every $\sim 170$ bases after retro-transcription with either poly(dT) or random hexamer primers (Supplemental Figure 3B). However, when total RNAs were retrotranscribed, an additional band with an approximate size of 50 bases was amplified. The same band is observed in control conditions (-RT, and -cDNA; Supplemental Figure 3B). The difference between profiles between the assay (poly(dT) and random hexamers) and controls ( -RT , and -cDNA ) indicated that cenRNA\#4 is poly-adenylated as well (Supplemental Figure 3B).

It has recently been reported in Xenopus (17), that centromeric RNAs appear to be spliced before they function to assist in CENP-A/CENP-C loading. We attempted to investigate whether human cenRNAs are processed using a $3^{\prime}-5$ ' RACE experiment; however, these results were inconclusive. Thus, while we were unable to definitively conclude whether human centromeric RNAs undergo splicing, these data suggest that polyadenylation is a maturation step that cenRNAs undergo before they bind CENPA/HJURP complexes.

Down-regulation of centromeric RNAs leads to chromosome segregation defects.

In our earlier work, the down-regulation of consensus $\alpha$-satellite RNAs by shRNA treatment led to an accumulation of mitotic defects (19). Indeed, parallel and previous work in Drosophila, Xenopus, and mammals demonstrate that loss of centromeric RNAs leads to mitotic defects underpine by the loss of CENP-A and CENP-C (15,17-19,48). Here, in order to investigate the function of cenRNA\#4, we generated an shRNA construct designed against cenRNA\#4 and analyzed the outcomes of the downregulation of this transcript (Figure 4).

HeLa cells were transfected with the H3-GFP or shRNA constructs and treated with puromycin to select for transfected cells (Figure 4A). At Day 2, the efficiency of transfection was assessed by quantifying the percentage of cells expressing H3-GFP and by an RNA FISH approach (Supplemental Figure 4). The percentage of cells expressing $\alpha$-satellite RNAs or cenRNA\#4 ( $58 \%$ and $43 \%$, respectively) after transfection with a scrambled sequence was similar to non-transfected cells (Supplemental Figure 4C-D). Compared to cells transfected with scrambled shRNA, we observed a decrease in the number of cells expressing centromeric RNAs ( $58 \%$ versus $34 \%$ ) and cenRNA\#4 ( $43 \%$ versus $22 \%$ ), validating our approach of centromeric RNAs down-regulation (Supplemental Figure 4C-D). At Day 6, HeLa cells were synchronized at late mitosis - early G1 and stained for $\alpha$-tubulin and CENP-B to visualize the mitotic spindle and centromeres, respectively (Figure 4A). We next scored for phenotypes related to chromosome segregation defects (Figure 4B and Supplemental Figure 5A-B). Cells transfected with scrambled shRNA displayed $30 \%$ of phenotypes related to chromosome segregation defects (Figure 4B). This percentage is explained by the high level of chromosome instability of HeLa cells $(49,50)$. However, the down-regulation of $\alpha$-satellite transcripts ( $\alpha$-sat) increased this percentage up to $50 \%$, indicating the major role of these RNAs in the correct segregation of chromosomes (Figure 4B and Supplemental Figure 5B). Similarly, the proportion of cells with chromosome defects increase with cenRNA\#4 down-regulation (up to $45 \%$; Figure 4B and Supplemental Figure 5B). Overall, these data suggest that centromeric transcripts identified in these experiments are involved in faithful cell division.

## DISCUSSION

Previously, we and others have shown that transcription is required for proper centromere function in human cells and is limited to late mitosis - early G1 (19). Here, we characterize the origin, localization, and putative function of these centromere-derived long non-coding RNAs. High throughput CENP-A RIP-seq experiments revealed several novel transcripts (Figure 1), which were polyadenylated. Curiously, only $30-40 \%$ of HeLa cells had signal for cenRNAs (Figure 2). In addition, the number of foci per nucleus was also less than the number of centromeres per nucleus (Figure 2 and Figure 3). Furthermore, the $\alpha$-satellite RNAs and CENP-B foci were juxta-positioned (Figure 4), results that were recapitulated for chromosome-specific cenRNAs (cenRNA\#4). Finally, knocking-down a chromosome-specific cenRNA resulted in mitotic defects (Figure 4). Altogether, these data reveal cenRNAs from different chromosomes are important for genome stability.

One specific question emerges from our observations. Why are cenRNA FISH signals only found in $30-40 \%$ of the cells at early G1? We consider several possible explanations. The most plausible one is that the temporal window when cenRNAs are actively transcribed is very short, thus reducing the odds
of capturing the event by bright RNA FISH, as this requires fixing the cells. Consequently, this could mean that not all centromeres produce cenRNAs at precisely the same time. Another possibility is cenRNA molecules are long lived, and not required in high abundance, allowing the deposition of CENP-A over several cell cycles. Thus, only a fraction of the centromeres may need to undergo transcription per cell cycle, potentially sporadically. A third possibility is the very low abundance and unstable nature of cenRNAs might complicate the detection of all cenRNAs, except during active transcription, both by RIP-seq or RNA FISH. Finally, a fourth possible explanation is that cenRNAs could function both in cis and in trans. In other words, cenRNAs transcribed from one centromere are also involved in function at other centromeres. This interpretation would be consistent with the observation that most human centromeres consist of very similar $\alpha$-satellite sequences, thus mildly diverged sequences may not be sufficient to inhibit trans-localization or activity of cenRNAs. In this scenario, cenRNAs are either transported to other centromeres by chaperones or by diffusion of the RNA molecules. In the former case, the responsible chaperone, likely HJURP, remains to be identified. In the latter case, proximity would be a limiting factor. The closer another centromere is to the centromere producing the cenRNAs, the greater the likelihood that diffusion results in trans use of the cenRNAs. Indeed, a recent study used a novel method to analyze Hi-C data and showed that in human lymphoblastoid cells several centromeres are in close proximity, creating regulatory communities (51). Thus, our observation that there are less $\alpha$-satellite RNA FISH signals than centromere signals is consistent with the possibility of trans-acting cenRNA (Figure 5).

Past reports describe the importance of centromeric transcripts in chromosome stability (10-12,19,23). We show that down-regulating centromeric transcripts using $\alpha$-satellite consensus sequence shRNA decreases the level of expression of several specific cenRNAs, leading to CENP-A depletion and chromosome defects. One may argue that in a trans model, the down-regulation of one specific transcript should not lead to mitotic defects, as other cenRNAs will prevent the absence of the lost cenRNAs. However, the fine-tune regulation of transcription at centromeres can impede this rescue, by not re-adjusting the level of centromeric transcripts, leading to a decrease of the cenRNAs pool. Indeed, work on human artificial chromosomes suggest that the level of transcription at the centromere is balanced by post-translational modifications present at this chromatin domain, and not by cenRNAs themselves $(48,52)$. Indeed, too much transcription is just as deleterious for CENP-A assembly as is too little. One speculative interpretation is that over-production of HAC cenRNAs might result in transmigration of those HAC-cenRNAs to other centromeres, effectively diluting CENP-A at the HAC.

Thus, in this "Goldilocks" model, overexpression of cenRNAs might result in the concentration of cenRNA exceeding its titer, followed by mislocalization of surplus cenRNA. This mislocalization might be facilitated by histone chaperones other than $\operatorname{HJURP}(53,54)$, resulting in ectopic deposition of CENP-A $(53,55)$. Ectopic CENP-A nucleosomes have the intrinsic capacity to be sites of ectopic kinetochore formation, which in turn can result in dicentric chromosomes. Ectopic CENP-A has also been found in colorectal cancers and misexpression of other kinetochore components has recently been shown to correlate with poor prognosis in various cancers $(55,56)$. It will therefore be extremely interesting to study the relationship and co-dependence between over-expressed cenRNAs and other over-expressed centromere and kinetochore proteins.

Taken together, in this follow up report, we find that multiple cenRNAs are produced from various chromosomes, ranging in size from 300-2000 bases, and these transcripts were found to be polyadenylated and localized adjacent to functional centromeres. Furthermore, despite only $30 \%$ of cells showing cenRNA signal, knockdown of chromosome-specific cenRNAs resulted in accumulated mitotic defects. Future work will be necessary to pinpoint the mechanism by which these cenRNAs assist in CENP-A loading at centromeres. We can envision 4 models by which cenRNAs can assist in CENP-A localization. First, cenRNAs might serve as true honing sequences, using an RNA-DNA hybrid mechanism to help tether HJURP/CENP-A/H4 complexes to centromeric sequences; second, cenRNAs may be structurally involved in a pre-assembly complex that stabilizes or co-folds CENP$\mathrm{A} / \mathrm{H} 4$, thus acting as co-chaperone; third, cenRNAs may sequester or protect pre-assembly CENP$\mathrm{A} / \mathrm{H} 4$, preventing their fortuitious association with H 3 complexes, or H3-containing chromatin before they are temporally loaded onto centromeres. Finally, based on several reports of cenRNAs binding CENP-C, it is tempting to speculate that cenRNAs in a pre-assembly complex with CENP-A/H4 and HJURP only permit association of these complexes to "active" centromeres because cenRNAs have a preference for pre-existing CENP-C-chromatin bound molecules. In this final mechanism, which is speculative and will require rigorous testing, we suggest that cenRNAs may act as a genetic-epigenetic toggle, reinforcing CENP-A localization only to active centromeres, rather than just to centromeres which contain alpha satellite sequences. This model would also address a long standing mystery in the field, wherein non-homologous CENP-As from distant species, when expressed in human cells, can localize to and rescue the loss of human CENP-A (57). In the absence of a true genetic centromere in human cells, it is has been puzzling to consider how, for example, yeast CENP-A can associate with centromeres of a species removed by several million years of evolution. In this model, it can be imagined that because the chaperone HJURP may bind non-cognate CENP-As, and can presumably also bind cenRNAs arising from active centromeres, it provides a mechanism for exogenous CENPAs to localize, and rescue human CENP-A loss from centromeres. Indeed, if intra-chromosomal use of cenRNAs is the mechanism, this might have also have implications for the evolution of centromere DNAs. The centromeres of most species consist of one type of satellite DNA. One outstanding question remains how it is possible that the centromeres of all chromosomes consist of the same type of satellite DNA. It is tempting to speculate that some sort of transposition had to have occurred. For instance, there are centromere-specific transposable elements (TEs) and the centromeres of Arabidopsis thaliana, which are devoid of TEs, can be invaded by an LTR retrotransposon from A. lyrata (58). A recent study comparing centromeres from different Zea mays inbred lines showed that CENP-A repositioned, followed by invasion of a transposable element (59). Altogether, centromere-specific transposition events have been shown to occur in plants and furthermore the centromere-associated protein CENP-B has been domesticated from a pogo-like transposase twice $(60,61)$. The question that remains is, beyond the transposition events on evolutionary timescales, has transposition behavior been domesticated by centromeres via trans-acting cenRNAs. These, and other fascinating evolutionary and mechanistic questions discussed above, await future investigation.

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## FIGURE LEGENDS

Figure 1: New RNAs associated to CENP-A chromatin identified by RIP-seq are originating from centromeres. (A) Schematic of RIP-seq protocol. (B) Summary of downstream data analysis pipeline (described in detail in (28)). (C-E) Screenshots of read coverage from CENP-A RIP-seq experiments for each of three identified transcripts. Input and depth-normalized read depths are presented, arbitrary scale. (F) Characteristics of novel cenRNAs identified by RIP-seq. Higher-order repeat (HOR) classification for each transcript. Data include locus coordinates, size of the sequenced RNA, higher-order repeat (HOR) or closest matching, GenBank accession, current assembly array, and repeat supra-chromosomal family (SF). (G) Size distribution of 432 detected centromeric transcripts. (H) Chromosome distribution of 432 detected centromeric transcripts.

Figure 2: cenRNAs display discrete nuclear localization. (A) Long non-coding RNAs NEAT1 and MALAT1 and centromeric transcripts are observed by RNA FISH in early G1 synchronized HeLa cells. (B) The frequency of cells expressing NEAT1 and MALAT1 and centromeric transcripts observed in A was quantified and tabulated ( $\mathrm{N}=3$ ).

Figure 3: cenRNAs and CENP-B domains partially co-localized. (A) Schematic of the co-IF/RNA FISH experiment. ( $\mathrm{B} \& \mathrm{C}$ ) G1-synchronized HeLa cells are stained for CENP-B, as marker of centromeres and centromeric transcripts ( $\alpha$-satellite in B and cenRNA\#4 in C). Cells displaying an overlap of the IF and RNA signals were counted amongst cells expressing $\alpha$-satellite transcripts and cenRNA\#4. No signal was observed after RNase treatment (+RNase) ( $\mathrm{N}=3$ ).

Figure 4: The down-regulation of cenRNAs is accompanied with chromosome defects. (A) Schematic of the down-regulation of cenRNAs followed by co-IF experiment. (B) Transfected HeLa cells with either scrambled or $\alpha$-satellite or cenRNA\#4 shRNA are synchronized at late mitosis - early G1 and stained for CENP-B (marker of centromeres) and $\alpha$-tubulin (marker of mitotic spindle). Cells were counted and categorized for their chromosome defects $(\mathrm{N}=3)$.

Figure 5: Working model. In a cis model, specific cenRNAs are transcribed from one centromere and stay associated to this specific centromere, leading to chromosome defects (e.g., lagging chromosomes, chromatin bridge) of this exact chromosome and the loss of CENP-A at this centromere. On the other hand, in a trans model, a specific cenRNAs transcribed from one centromere will act on different chromosomes. Its loss will cause genome instability on different chromosomes.

Supplemental Figure 1: Description of centromeric transcripts identified by RIP-seq. (A) Sequence logos for the most abundant motif, in each of four subsets ( $\sim 100$ each) of putative centromeric transcript sequences. Motif length and significance as reported by MEME are indicated. (B-F) Pairwise percent identity matrix of 432 centromeric transcripts detected via CENP-A Ripseq. Percent identity is displayed in shades of grey, with lighter shades indicating more similar. Hierarchical clustering was performed, which separates the transcripts into four groups (indicated at left), based on the four top most dendrogram branch points. A color code (right) indicates the chromosome of origin for each transcript. The three transcripts described in detail in this work are indicated at right.

Supplemental Figure 2: cenRNAs are not observed after RNase treatment. As in figure 3, RNAs were stained by RNA FISH in early G1 synchronized HeLa cells after treatment with RNase A treatment. A long exposure staining is shown to highlight the absence of RNA FISH signal ( $\mathrm{N}=3$ ).

Supplemental Figure 3: RNAs transcribed from centromeres are poly-adenylated. (A) Using primers designed against centromeric $\alpha$-satellite, total RNAs were amplified after retro-transcription with either poly-(dT) or random hexamer primers. (B) As in A, total RNAs were retro-transcribed and amplified with primers designed against cenRNA\#4. bp: base pairs; MW: molecular weight (50bp ladder); -RT: no RT; -DNA: no cDNA ( $\mathrm{N}=3$ ).

Supplemental figure 4: cenRNAs are down-regulated by shRNA approach. (A) Schematic of the RNA FISH and IF experiments. (B) HeLa cells are fixed and observed under microcope. H3-GFP positive cells are tabulated. (C \& D) HeLa cells are stained for $\alpha$-satellite transcripts (B) or cenRNA\#4 (C) two days post-transfection with an shRNA constructs. Cells displaying an RNA signal were counted and tabulated (graphs on the right) ( $\mathrm{N}=4$ minimum).

Supplemental figure 5: cenRNAs depletion leads to chromosome defects. (A) Schematic of the down-regulation of cenRNAs followed by co-IF experiment. (B) Transfected HeLa cells with either scrambled or $\alpha$-satellite or cenRNA\#4 shRNA are synchronized at late mitosis - early G1 and stained for CENP-B (marker of centromeres) and $\alpha$-tubulin (marker of mitotic spindle). Cells were counted and categorized for their chromosome defects ( $\mathrm{N}=3$ ).

Figure 1:
A


Alignment and analysis

RNA-Protein complex
B


cenRNA\#2


F

| ID | Locus <br> (hg38 coordinates) | Size <br> (bp) | HOR | GenBank | Array | Supra- <br> chromosomal <br> family |
| :--- | :--- | :---: | :--- | :--- | :--- | :--- |
| CenRNA\#2 | chr3:93470360- <br> 93470800 | 440 | DSZ1 | GJ211871.1 | cen3_1 | SF1 |
| CenRNA\#3 | chr17:23016255- <br> 23016556 | 301 | D17Z1 (97\%) | GJ212053.1 | cen17_2 | SF3 |
| CenRNA\#4 | chr17:26603730- <br> 26604659 | 929 | D17Z1 (98\%) | GJ212055.1 | cen17_3 | SF3 |



H

Figure 2:
A.


至

B.

| RNA | \% of cells <br> with an RNA <br> signal | Standard <br> deviation | Number of <br> cells counted |
| :--- | :--- | :--- | :--- |
| NEAT | 97.37 | 0.94 | 731 |
| MALAT1 | 84.42 | 6.04 | 726 |
| $\alpha$-satellite | 34.02 | 7.62 | 622 |
| cenRNA\#2 | 3.65 | 2.38 | 685 |
| cenRNA\#3 | 27.68 | 18.66 | 698 |
| cenRNA\#4 | 37.37 | 15.30 | 697 |

Figure 3:
A.

B.

-RNase
$73.7 \%+/-4.7 \%$ colocalized $\mathrm{n}=116$

+RNase

C.


Figure 4:
A.

B.


Figure 5:

CENP-A loss at chromosome 17


Supplemental Figure 1:
A.

Set $1, \mathrm{p}=2.7 \mathrm{e}-5459,113 \mathrm{bp}$

## Set 2, p=8.7-4695,113bp <br> Set 3, p=44e-3491, 88bp <br> Set $4, \mathrm{p}=1.6 \mathrm{e}-3541,92 \mathrm{bp}$ <br> 

E.

B.

D.

F.


Supplemental Figure 2


Supplemental Figure 3:


Supplemental Figure 4:
A.

B.

DAPI
H3-GFP
Merge


Transfection efficiency: $82.2 \% \pm 3.1 \% ~(\mathrm{~N}=5)$
C.

D.



Supplemental Figure 5:
A.



Supplemental Table 1: List of antibodies.

| Target Protein | Reference | Manufacturer | Method |
| :--- | :--- | :--- | :--- |
| CENP-A "3-19" | ab13939 | Abcam | RNA Immuno-Precipitation - <br> sequencing, Immuno-Fluorescence |
| CENP-B "H65" | sc-22788 | Santa Cruz | Immuno-Fluorescence |
| $\alpha$-Tubulin <br> "DM1A" | 62204 | Thermo Fisher <br> Scientific | Immuno-Fluorescence |

Supplemental Table 2: List of shRNA sequence.

| Target Sequence | Sequence (5' to 3') |
| :--- | :--- |
| Scrambled | GCACTACCAGAGCTAACTCAGATAGTACT |
| $\alpha$-satellite A | TGTGTGCATTCAACTCACAGAGTTG |
| $\alpha$-satellite B | CAACTCACAGAGTTGAACCTTCCTT |
| cenRNA\#4 A | GATGACTGCATTCAACTCACGGAGTTGAA |
| cenRNA\#4 B | CACCTCACAGAGTTGACCATTCCTATTGA |

Supplemental Table 3: List of primer sequence.

| Target Sequence |  | Sequence (5' to 3') | Method |
| :--- | :--- | :--- | :--- |
| $\alpha$-satellite SetA | Forward | TGCATTCAACTCACAGAGTTGAAC | PCR |
|  | Reverse | CATCACAAAGAAGTTTCTGAGAATGC | PCR |
| $\alpha$-satellite SetB | Forward | CAACTCACAGAGTTGAACCTTCCTT | PCR |
|  | Reverse | AGTTGAATGCACACATCACAAAGA | PCR |
| cenRNA\#4 SetA | Forward | ACTCCTTTTGAGAGCGCAGT | PCR |
|  | Reverse | GGTGCAGTTATCTCGTTTCCA | PCR |
| cenRNA\#4 SetB | Forward | CTCTCTTTCTGTGGCATCTG | PCR |
|  | Reverse | GAATGGTCAACTCTGTGAGG | PCR |
| GAPDH | Forward | AGTCAACGGGTTTGGTCGTAT | PCR |
|  | Reverse | CTGCAAATGAGCCCCAGCC | PCR |

key tracking_id
1 CenRNA2
2 CenRNA3
3 cenRNA:chr17:26594525-26594960
4 CenRNA4
5 cenRNA:chr17:24150840-24151314
6 cenRNA:chr19:25422901-25423243
7 cenRNA:chr12:35011195-35011560
8 cenRNA:chr5:47491561-47491892
9 cenRNA:chr19:25600817-25601375
10 cenRNA:chr17:24740075-24740585
11 cenRNA:chr19:26750190-26750573
12 cenRNA:chr20:27194762-27195193
13 cenRNA:chr5:48001328-48001892
14 cenRNA:chr17:26098145-26098474
15 cenRNA:chr5:48535895-48536223
16 cenRNA:chr10:40924813-40925129
17 cenRNA:chr12:36782697-36783180
18 cenRNA:chr4:50562740-50563124
19 cenRNA:chr20:28313055-28313356
20 cenRNA:chr11:51814030-51814362
21 cenRNA:chr18:16740369-16740720
22 cenRNA:chr17:25033865-25034240
23 cenRNA:chr12:36513965-36514305
24 cenRNA:chr1:123518947-123519369
25 cenRNA:chr17:24187861-24188440
26 cenRNA:chr12:35427176-35427564
27 cenRNA:chr19:27146703-27147147
28 cenRNA:chr15:18780386-18781210
29 cenRNA:chr10:41013772-41014155
30 cenRNA:chr10:41068409-41068823
31 cenRNA:chr2:92598948-92599257
32 cenRNA:chr4:51107215-51107566
33 cenRNA:chr11:53631485-53631880
34 cenRNA:chr18:15885398-15885724
35 cenRNA:chr22:14878202-14878530
36 cenRNA:chr2:93866822-93867203
37 cenRNA:chr10:39979064-39979448
38 cenRNA:chr19:26880103-26880489
39 cenRNA:chr11:54102184-54102514
40 cenRNA:chr2:92655343-92655754
41 cenRNA:chr1:123128673-123129060

| locus | chr | length |
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| chr17:26603730-26604659 | chr17 | 929 |
| chr17:24150840-24151314 | chr17 | 474 |
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| chr5:47491561-47491892 | chr5 | 331 |
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chr11:51092592-51093123 chr11 531
chr19:25224641-25225090 chr19 449
chr11:53375117-53375704 chr11 587
chr5:49367931-49369179 chr5 1248
chr17:26548702-26549136 chr17 434
chr5:48893293-48893658 chr5 365
chr4:51080855-51081274 chr4 419
chr11:53916809-53917157 chr11 348
chr12:37081816-37082218 chr12 402
chr4:51434565-51435109 chr4 544
chr10:40806906-40807345 chr10 439
chr17:23055469-23055837 chr17 368
chr17:24364189-24364629 chr17 440
chr5:48540120-48540472 chr5 352
chr19:24934236-24934645 chr19 409
chr5:47797583-47797937 chr5 354
chr19:27162721-27163465 chr19 744
chr5:46985117-46985548 chr5 431
chr10:41176757-41177282 chr10 525
chr11:53980600-53981014 chr11 414
chr7:60544383-60544872 chr7 489
chr5:48547165-48547503 chr5 338
chr10:40105175-40105966 chr10 791
chr11:54040087-54040654 chr11 567
chr11:53564416-53564870 chr11 454
chr12:35619403-35619762 chr12 359
chr21:12739650-12740106 chr21 456
chr9:44621024-44621538 chr9 514
chr11:51982309-51982862 chr11 553
chr5:50036126-50036487 chr5 361
chr5:49543637-49544426 chr5 789
chr1:122599682-122600046 chr1 364
chr9:43800776-43801222 chr9 446
chrX:61425086-61425572 chrX 486
chr3:92951512-92951939 chr3 427
chr16:38019280-38019628 chr16 348
chr1:122510753-122511060 chr1 307
chr12:36547531-36547967 chr12 436

168 cenRNA:chr11:52759524-52759898 169 cenRNA:chr10:41130545-41130961 170 cenRNA:chr5:48333691-48334149 171 cenRNA:chr12:35770494-35770890 172 cenRNA:chr9:44895369-44895808 173 cenRNA:chr3:92358403-92358821 174 cenRNA:chr10:41345572-41345991 175 cenRNA:chr12:35965549-35967067 176 cenRNA:chr7:60397425-60397866 177 cenRNA:chr1:122462444-122462864 178 cenRNA:chr16:37516257-37516613 179 cenRNA:chr11:53838565-53838943 180 cenRNA:chr17:23009293-23009927 181 cenRNA:chr11:53600894-53601337 182 cenRNA:chr20:26582901-26583258 183 cenRNA:chr20:28548431-28549646 184 cenRNA:chr11:52679616-52680919 185 cenRNA:chr1:124253782-124254140 186 cenRNA:chr4:49889166-49889613 187 cenRNA:chr3:93133399-93133935 188 cenRNA:chr2:93224579-93225006 189 cenRNA:chr11:53153976-53154291 190 cenRNA:chr11:52697347-52697708 191 cenRNA:chr11:52795266-52796417 192 cenRNA:chr5:48205766-48206194 193 cenRNA:chr1:124505506-124505912 194 cenRNA:chr11:52470580-52470919 195 cenRNA:chr20:27603311-27603762 196 cenRNA:chr5:48183312-48183764 197 cenRNA:chr11:52049738-52050078 198 cenRNA:chr5:48245126-48245649 199 cenRNA:chr21:12552940-12553283 200 cenRNA:chr17:24598540-24599205 201 cenRNA:chr11:52447518-52447886 202 cenRNA:chr11:53765538-53765906 203 cenRNA:chr11:53554142-53554649 204 cenRNA:chr20:26781218-26781610 205 cenRNA:chr3:91824394-91824786 206 cenRNA:chr4:49858740-49859432 207 cenRNA:chr17:25442364-25442921 208 cenRNA:chr3:92618206-92618577 209 cenRNA:chr11:54019720-54021679

| chr11:52759524-52759898 | chr11 | 374 |
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| chr10:41130545-41130961 | chr10 | 416 |
| chr5:48333691-48334149 | chr5 | 458 |
| chr12:35770494-35770890 | chr12 | 396 |
| chr9:44895369-44895808 | chr9 | 439 |
| chr3:92358403-92358821 | chr3 | 418 |
| chr10:41345572-41345991 | chr10 | 419 |
| chr12:35965549-35967067 | chr12 | 1518 |
| chr7:60397425-60397866 | chr7 | 441 |
| chr1:122462444-122462864 | chr1 | 420 |
| chr16:37516257-37516613 | chr16 | 356 |
| chr11:53838565-53838943 | chr11 | 378 |
| chr17:23009293-23009927 | chr17 | 634 |
| chr11:53600894-53601337 | chr11 | 443 |
| chr20:26582901-26583258 | chr20 | 357 |
| chr20:28548431-28549646 | chr20 | 1215 |
| chr11:52679616-52680919 | chr11 | 1303 |
| chr1:124253782-124254140 | chr1 | 358 |
| chr4:49889166-49889613 | chr4 | 447 |
| chr3:93133399-93133935 | chr3 | 536 |
| chr2:93224579-93225006 | chr2 | 427 |
| chr11:53153976-53154291 | chr11 | 315 |
| chr11:52697347-52697708 | chr11 | 361 |
| chr11:52795266-52796417 | chr11 | 1151 |
| chr5:48205766-48206194 | chr5 | 428 |
| chr1:124505506-124505912 | chr1 | 406 |
| chr11:52470580-52470919 | chr11 | 339 |
| chr20:27603311-27603762 | chr20 | 451 |
| chr5:48183312-48183764 | chr5 | 452 |
| chr11:52049738-52050078 | chr11 | 340 |
| chr5:48245126-48245649 | chr5 | 523 |
| chr21:12552940-12553283 | chr21 | 343 |
| chr17:24598540-24599205 | chr17 | 665 |
| chr11:52447518-52447886 | chr11 | 368 |
| chr11:53765538-53765906 | chr11 | 368 |
| chr11:53554142-53554649 | chr11 | 507 |
| chr20:26781218-26781610 | chr20 | 392 |
| chr3:91824394-91824786 | chr3 | 392 |
| chr4:49858740-49859432 | chr4 | 692 |
| chr17:25442364-25442921 | chr17 | 557 |
| chr3:92618206-92618577 | chr3 | 371 |
| chr11:54019720-54021679 | chr11 | 1959 |

210 cenRNA:chr17:22815930-22816652 211 cenRNA:chr18:15695333-15695780 212 cenRNA:chr11:52872607-52872958 213 cenRNA:chr15:19488615-19488915 214 cenRNA:chr12:36465198-36465550 215 cenRNA:chr11:54251259-54252721 216 cenRNA:chr11:51683118-51683569 217 cenRNA:chr11:52682213-52682789 218 cenRNA:chr10:41198004-41198850 219 cenRNA:chr11:51966780-51967479 220 cenRNA:chr5:48036665-48036995 221 cenRNA:chr20:27814202-27814858 222 cenRNA:chr5:49133860-49134317 223 cenRNA:chr20:26898110-26898493 224 cenRNA:chr1:124338393-124338725 225 cenRNA:chr9:43563175-43563885 226 cenRNA:chr1:124531006-124531641 227 cenRNA:chr3:92585513-92586450 228 cenRNA:chr11:52708236-52709536 229 cenRNA:chr1:123057503-123057810 230 cenRNA:chr11:53849046-53849433 231 cenRNA:chr10:41217318-41217731 232 cenRNA:chr11:51289660-51290100 233 cenRNA:chr5:47735127-47735516 234 cenRNA:chr17:26006654-26007276 235 cenRNA:chr1:123459117-123459558 236 cenRNA:chr12:36488356-36488693 237 cenRNA:chr11:52011311-52011885 238 cenRNA:chr17:23973175-23973856 239 cenRNA:chr17:22941094-22941749 240 cenRNA:chr20:27854938-27855543 241 cenRNA:chr1:122725297-122725665 242 cenRNA:chr19:26972753-26973390 243 cenRNA:chr11:54335435-54336609 244 cenRNA:chr11:52588727-52589284 245 cenRNA:chr12:36228334-36230026 246 cenRNA:chr9:45412381-45412834 247 cenRNA:chr7:58956541-58956967 248 cenRNA:chr3:91886337-91886846 249 cenRNA:chr3:91811133-91811533 250 cenRNA:chr4:50842454-50842965 251 cenRNA:chr17:24526204-24526549

| chr17:22815930-22816652 | chr17 | 722 |
| :--- | :--- | ---: |
| chr18:15695333-15695780 | chr18 | 447 |
| chr11:52872607-52872958 | chr11 | 351 |
| chr15:19488615-19488915 | chr15 | 300 |
| chr12:36465198-36465550 | chr12 | 352 |
| chr11:54251259-54252721 | chr11 | 1462 |
| chr11:51683118-51683569 | chr11 | 451 |
| chr11:52682213-52682789 | chr11 | 576 |
| chr10:41198004-41198850 | chr10 | 846 |
| chr11:51966780-51967479 | chr11 | 699 |
| chr5:48036665-48036995 | chr5 | 330 |
| chr20:27814202-27814858 | chr20 | 656 |
| chr5:49133860-49134317 | chr5 | 457 |
| chr20:26898110-26898493 | chr20 | 383 |
| chr1:124338393-124338725 | chr1 | 332 |
| chr9:43563175-43563885 | chr9 | 710 |
| chr1:124531006-124531641 | chr1 | 635 |
| chr3:92585513-92586450 | chr3 | 937 |
| chr11:52708236-52709536 | chr11 | 1300 |
| chr1:123057503-123057810 | chr1 | 307 |
| chr11:53849046-53849433 | chr11 | 387 |
| chr10:41217318-41217731 | chr10 | 413 |
| chr11:51289660-51290100 | chr11 | 440 |
| chr5:47735127-47735516 | chr5 | 389 |
| chr17:26006654-26007276 | chr17 | 622 |
| chr1:123459117-123459558 | chr1 | 441 |
| chr12:36488356-36488693 | chr12 | 337 |
| chr11:52011311-52011885 | chr11 | 574 |
| chr17:23973175-23973856 | chr17 | 681 |
| chr17:22941094-22941749 | chr17 | 655 |
| chr20:27854938-27855543 | chr20 | 605 |
| chr1:122725297-122725665 | chr1 | 368 |
| chr4:50842454-50842965 | chr4 | 511 |
| chr17:24526204-24526549 | chr17 | 345 |
| chr11:543372753-26973390 | chr19 | 637 |
| chr11:52588727-525892854 | chr11 | 1174 |
| chr12:36228334-36230026 | chr12 | 557 |
| chr9:45412381-45412834 | chr9 | 1692 |

252 cenRNA:chr19:26602103-26602448
253 cenRNA:chr11:54272528-54273095
254 cenRNA:chr11:53658264-53658722
255 cenRNA:chr11:52306198-52306934
256 cenRNA:chr9:43423820-43424501
257 cenRNA:chr3:93328436-93328978
258 cenRNA:chr11:52465481-52466218
259 cenRNA:chr19:25119081-25120272
260 cenRNA:chr12:36814656-36815679
261 cenRNA:chr5:47926212-47926617
262 cenRNA:chr1:123555932-123556621
263 cenRNA:chr19:25072669-25073018
264 cenRNA:chr3:92396509-92396916
265 cenRNA:chr3:92666889-92667297
266 cenRNA:chr4:50188823-50189231
267 cenRNA:chr4:51132967-51133861
268 cenRNA:chr17:26326121-26326787
269 cenRNA:chr11:51560455-51561295
270 cenRNA:chr19:25779809-25780276
271 cenRNA:chr4:50707213-50707594
272 cenRNA:chr5:48377230-48377727
273 cenRNA:chr9:44499269-44499824
274 cenRNA:chr7:59542160-59542571
275 cenRNA:chr19:26935495-26935993
276 cenRNA:chr1:122138610-122138932
277 cenRNA:chr11:52750006-52750447
278 cenRNA:chr1:123979957-123980370
279 cenRNA:chr11:53794359-53794772
280 cenRNA:chr12:36854676-36855089
281 cenRNA:chr18:19555252-19555606
282 cenRNA:chr11:51641632-51642075
283 cenRNA:chr5:48622293-48622971
284 cenRNA:chr19:25546424-25547308
285 cenRNA:chr3:92827630-92827985
286 cenRNA:chr11:52285364-52286016
287 cenRNA:chr11:53116440-53117183
288 cenRNA:chr4:50747682-50748128
289 cenRNA:chr9:44251165-44251701
290 cenRNA:chr1:122761559-122761976
291 cenRNA:chr4:51719445-51720071
292 cenRNA:chr11:52468696-52469145
293 cenRNA:chr20:27794182-27795173

| chr19:26602103-26602448 | chr19 | 345 |
| :---: | :---: | :---: |
| chr11:54272528-54273095 | chr11 | 567 |
| chr11:53658264-53658722 | chr11 | 458 |
| chr11:52306198-52306934 | chr11 | 736 |
| chr9:43423820-43424501 | chr9 | 681 |
| chr3:93328436-93328978 | chr3 | 542 |
| chr11:52465481-52466218 | chr11 | 737 |
| chr19:25119081-25120272 | chr19 | 1191 |
| chr12:36814656-36815679 | chr12 | 1023 |
| chr5:47926212-47926617 | chr5 | 405 |
| chr1:123555932-123556621 | chr1 | 689 |
| chr19:25072669-25073018 | chr19 | 349 |
| chr3:92396509-92396916 | chr3 | 407 |
| chr3:92666889-92667297 | chr3 | 408 |
| chr4:50188823-50189231 | chr4 | 408 |
| chr4:51132967-51133861 | chr4 | 894 |
| chr17:26326121-26326787 | chr17 | 666 |
| chr11:51560455-51561295 | chr11 | 840 |
| chr19:25779809-25780276 | chr19 | 467 |
| chr4:50707213-50707594 | chr4 | 381 |
| chr5:48377230-48377727 | chr5 | 497 |
| chr9:44499269-44499824 | chr9 | 555 |
| chr7:59542160-59542571 | chr7 | 411 |
| chr19:26935495-26935993 | chr19 | 498 |
| chr1:122138610-122138932 | chr1 | 322 |
| chr11:52750006-52750447 | chr11 | 441 |
| chr1:123979957-123980370 | chr1 | 413 |
| chr11:53794359-53794772 | chr11 | 413 |
| chr12:36854676-36855089 | chr12 | 413 |
| chr18:19555252-19555606 | chr18 | 354 |
| chr11:51641632-51642075 | chr11 | 443 |
| chr5:48622293-48622971 | chr5 | 678 |
| chr19:25546424-25547308 | chr19 | 884 |
| chr3:92827630-92827985 | chr3 | 355 |
| chr11:52285364-52286016 | chr11 | 652 |
| chr11:53116440-53117183 | chr11 | 743 |
| chr4:50747682-50748128 | chr4 | 446 |
| chr9:44251165-44251701 | chr9 | 536 |
| chr1:122761559-122761976 | chr1 | 417 |
| chr4:51719445-51720071 | chr4 | 626 |
| chr11:52468696-52469145 | chr11 | 449 |
| chr20:27794182-27795173 | chr20 | 991 |

294 cenRNA:chr19:26247238-26247657
295 cenRNA:chr11:53603618-53604218 296 cenRNA:chr11:53931742-53932704 297 cenRNA:chr1:122726785-122727112 298 cenRNA:chr1:124555142-124555592 299 cenRNA:chr12:35681712-35682253 300 cenRNA:chr11:51496033-51496453 301 cenRNA:chr5:48449166-48449862 302 cenRNA:chr11:52748519-52749461 303 cenRNA:chr17:23153815-23155037 304 cenRNA:chr11:53525770-53526749 305 cenRNA:chr11:52391351-52392022 306 cenRNA:chr5:48647733-48648189 307 cenRNA:chr15:17537697-17538370 308 cenRNA:chr11:52347105-52348212 309 cenRNA:chr12:35690131-35690774 310 cenRNA:chr5:49747416-49747904 311 cenRNA:chr9:44278748-44279361 312 cenRNA:chr1:123557258-123557685 313 cenRNA:chr17:24953969-24954553 314 cenRNA:chr11:51441676-51442072 315 cenRNA:chr1:123610460-123611045 316 cenRNA:chr15:19697940-19698368 317 cenRNA:chr1:124064764-124065161 318 cenRNA:chr11:52345163-52345592 319 cenRNA:chr20:28299579-28300135 320 cenRNA:chr1:122899028-122899394 321 cenRNA:chr3:93474763-93475288 322 cenRNA:chr17:25842790-25843442 323 cenRNA:chrX:61670116-61670515 324 cenRNA:chr20:27438283-27438650 325 cenRNA:chr19:25581321-25581621 326 cenRNA:chr4:49756355-49757298 327 cenRNA:chr11:51143036-51143500 328 cenRNA:chr11:52627854-52628287 329 cenRNA:chr11:53861602-53861971 330 cenRNA:chr3:92366738-92367270 331 cenRNA:chr19:24908795-24909492 332 cenRNA:chr1:123346957-123347459 333 cenRNA:chr20:28317146-28317550 334 cenRNA:chr11:51141091-51141561 335 cenRNA:chr17:23103073-23103511

| chr19:26247238-26247657 | chr19 | 419 |
| :---: | :---: | :---: |
| chr11:53603618-53604218 | chr11 | 600 |
| chr11:53931742-53932704 | chr11 | 962 |
| chr1:122726785-122727112 | chr1 | 327 |
| chr1:124555142-124555592 | chr1 | 450 |
| chr12:35681712-35682253 | chr12 | 541 |
| chr11:51496033-51496453 | chr11 | 420 |
| chr5:48449166-48449862 | chr5 | 696 |
| chr11:52748519-52749461 | chr11 | 942 |
| chr17:23153815-23155037 | chr17 | 1222 |
| chr11:53525770-53526749 | chr11 | 979 |
| chr11:52391351-52392022 | chr11 | 671 |
| chr5:48647733-48648189 | chr5 | 456 |
| chr15:17537697-17538370 | chr15 | 673 |
| chr11:52347105-52348212 | chr11 | 1107 |
| chr12:35690131-35690774 | chr12 | 643 |
| chr5:49747416-49747904 | chr5 | 488 |
| chr9:44278748-44279361 | chr9 | 613 |
| chr1:123557258-123557685 | chr1 | 427 |
| chr17:24953969-24954553 | chr17 | 584 |
| chr11:51441676-51442072 | chr11 | 396 |
| chr1:123610460-123611045 | chr1 | 585 |
| chr15:19697940-19698368 | chr15 | 428 |
| chr1:124064764-124065161 | chr1 | 397 |
| chr11:52345163-52345592 | chr11 | 429 |
| chr20:28299579-28300135 | chr20 | 556 |
| chr1:122899028-122899394 | chr1 | 366 |
| chr3:93474763-93475288 | chr3 | 525 |
| chr17:25842790-25843442 | chr17 | 652 |
| chrX:61670116-61670515 | chrX | 399 |
| chr20:27438283-27438650 | chr20 | 367 |
| chr19:25581321-25581621 | chr19 | 300 |
| chr4:49756355-49757298 | chr4 | 943 |
| chr11:51143036-51143500 | chr11 | 464 |
| chr11:52627854-52628287 | chr11 | 433 |
| chr11:53861602-53861971 | chr11 | 369 |
| chr3:92366738-92367270 | chr3 | 532 |
| chr19:24908795-24909492 | chr19 | 697 |
| chr1:123346957-123347459 | chr1 | 502 |
| chr20:28317146-28317550 | chr20 | 404 |
| chr11:51141091-51141561 | chr11 | 470 |
| chr17:23103073-23103511 | chr17 | 438 |

chr11:53603618-53604218 chr11 600 962 327 450 541 420 696 942 1222 979 671 456 673 1107 643 488 613 427 584 396 585 428 397 429 556 366 525 652 399 367 300 943 464 433 369 532 697 502 404 470 438

336 cenRNA:chr4:49718514-49718886
337 cenRNA:chr11:54098805-54099144 338 cenRNA:chr5:49511240-49512044 339 cenRNA:chr11:53251143-53251818 340 cenRNA:chr11:54301082-54302262 341 cenRNA:chr3:91658284-91658895
342 cenRNA:chr17:24692478-24692854 343 cenRNA:chr11:52737387-52737898 344 cenRNA:chr11:53825053-53825395 345 cenRNA:chr3:93230726-93231138 346 cenRNA:chr11:52990656-52991239 347 cenRNA:chr19:26458002-26458449
348 cenRNA:chr11:54237176-54238210 349 cenRNA:chr1:124500811-124501365 350 cenRNA:chr11:52082783-52083338 351 cenRNA:chr7:59085472-59085993 352 cenRNA:chr11:54123668-54124051 353 cenRNA:chr17:23177999-23178489 354 cenRNA:chr17:23133938-23134784 355 cenRNA:chr11:52830623-52831542 356 cenRNA:chr11:53295221-53295856 357 cenRNA:chr10:41447011-41447647 358 cenRNA:chr11:52384360-52384961 359 cenRNA:chr11:53191148-53191571 360 cenRNA:chr16:38016735-38017158 361 cenRNA:chr11:54189530-54190313 362 cenRNA:chr7:59898072-59898749 363 cenRNA:chr3:92888929-92889860 364 cenRNA:chr12:35992710-35993895 365 cenRNA:chr11:53304574-53305365 366 cenRNA:chr10:41493821-41494758 367 cenRNA:chr11:52614908-52615590 368 cenRNA:chr11:53637381-53637808 369 cenRNA:chr11:52778775-52780298 370 cenRNA:chr12:36522876-36524738 371 cenRNA:chr8:44594360-44595046 372 cenRNA:chr12:34998907-34999446 373 cenRNA:chr17:26270660-26271274 374 cenRNA:chr11:52806198-52806850 375 cenRNA:chr18:18528554-18528947 376 cenRNA:chr7:59669642-59670334 377 cenRNA:chr7:58378749-58379667

| chr4:49718514-49718886 | chr4 | 372 |
| :---: | :---: | :---: |
| chr11:54098805-54099144 | chr11 | 339 |
| chr5:49511240-49512044 | chr5 | 804 |
| chr11:53251143-53251818 | chr11 | 675 |
| chr11:54301082-54302262 | chr11 | 1180 |
| chr3:91658284-91658895 | chr3 | 611 |
| chr17:24692478-24692854 | chr17 | 376 |
| chr11:52737387-52737898 | chr11 | 511 |
| chr11:53825053-53825395 | chr11 | 342 |
| chr3:93230726-93231138 | chr3 | 412 |
| chr11:52990656-52991239 | chr11 | 583 |
| chr19:26458002-26458449 | chr19 | 447 |
| chr11:54237176-54238210 | chr11 | 1034 |
| chr1:124500811-124501365 | chr1 | 554 |
| chr11:52082783-52083338 | chr11 | 555 |
| chr7:59085472-59085993 | chr7 | 521 |
| chr11:54123668-54124051 | chr11 | 383 |
| chr17:23177999-23178489 | chr17 | 490 |
| chr17:23133938-23134784 | chr17 | 846 |
| chr11:52830623-52831542 | chr11 | 919 |
| chr11:53295221-53295856 | chr11 | 635 |
| chr10:41447011-41447647 | chr10 | 636 |
| chr11:52384360-52384961 | chr11 | 601 |
| chr11:53191148-53191571 | chr11 | 423 |
| chr16:38016735-38017158 | chr16 | 423 |
| chr11:54189530-54190313 | chr11 | 783 |
| chr7:59898072-59898749 | chr7 | 677 |
| chr3:92888929-92889860 | chr3 | 931 |
| chr12:35992710-35993895 | chr12 | 1185 |
| chr11:53304574-53305365 | chr11 | 791 |
| chr10:41493821-41494758 | chr10 | 937 |
| chr11:52614908-52615590 | chr11 | 682 |
| chr11:53637381-53637808 | chr11 | 427 |
| chr11:52778775-52780298 | chr11 | 1523 |
| chr12:36522876-36524738 | chr12 | 1862 |
| chr8:44594360-44595046 | chr8 | 686 |
| chr12:34998907-34999446 | chr12 | 539 |
| chr17:26270660-26271274 | chr17 | 614 |
| chr11:52806198-52806850 | chr11 | 652 |
| chr18:18528554-18528947 | chr18 | 393 |
| chr7:59669642-59670334 | chr7 | 692 |
| chr7:58378749-58379667 | chr7 | 918 |

378 cenRNA:chr12:36531171-36533621 379 cenRNA:chr18:15917121-15917555 380 cenRNA:chr11:54289548-54290286 381 cenRNA:chr2:94046568-94046928 382 cenRNA:chr11:51678914-51679313 383 cenRNA:chr17:24809917-24810585 384 cenRNA:chr3:91009604-91009965 385 cenRNA:chr17:26266579-26266979 386 cenRNA:chr3:93282114-93283208 387 cenRNA:chr11:51528828-51529930 388 cenRNA:chr16:36345826-36346773 389 cenRNA:chr20:28336851-28337254 390 cenRNA:chr5:49407661-49408105 391 cenRNA:chr20:27075758-27076203 392 cenRNA:chr11:53296905-53297311 393 cenRNA:chr20:28041136-28042216 394 cenRNA:chr12:36366027-36366473 395 cenRNA:chr15:19095211-19095856 396 cenRNA:chr22:14910304-14910711 397 cenRNA:chr17:25597444-25598092 398 cenRNA:chr4:51235620-51235988 399 cenRNA:chr11:51276659-51277471 400 cenRNA:chr7:59793816-59794226 401 cenRNA:chr11:51176830-51177362 402 cenRNA:chr11:51798688-51799307 403 cenRNA:chr17:24882900-24883521 404 cenRNA:chr4:50608432-50609053 405 cenRNA:chr11:54094659-54095032 406 cenRNA:chr1:122933713-122934128 407 cenRNA:chr11:52670738-52671692 408 cenRNA:chr1:124754461-124754918 409 cenRNA:chr11:52868853-52869562 410 cenRNA:chr11:53922752-53923127 411 cenRNA:chr5:48471029-48471404 412 cenRNA:chr5:47565226-47565644 413 cenRNA:chr3:93151408-93152289 414 cenRNA:chrX:61063675-61064395 415 cenRNA:chr17:23206055-23206478 416 cenRNA:chr15:19059864-19060545 417 cenRNA:chr15:19433431-19433767 418 cenRNA:chr11:52647375-52647973 419 cenRNA:chr9:44436592-44437062

| chr12:36531171-36533621 | chr12 | 2450 |
| :---: | :---: | :---: |
| chr18:15917121-15917555 | chr18 | 434 |
| chr11:54289548-54290286 | chr11 | 738 |
| chr2:94046568-94046928 | chr2 | 360 |
| chr11:51678914-51679313 | chr11 | 399 |
| chr17:24809917-24810585 | chr17 | 668 |
| chr3:91009604-91009965 | chr3 | 361 |
| chr17:26266579-26266979 | chr17 | 400 |
| chr3:93282114-93283208 | chr3 | 1094 |
| chr11:51528828-51529930 | chr11 | 1102 |
| chr16:36345826-36346773 | chr16 | 947 |
| chr20:28336851-28337254 | chr20 | 403 |
| chr5:49407661-49408105 | chr5 | 444 |
| chr20:27075758-27076203 | chr20 | 445 |
| chr11:53296905-53297311 | chr11 | 406 |
| chr20:28041136-28042216 | chr20 | 1080 |
| chr12:36366027-36366473 | chr12 | 446 |
| chr15:19095211-19095856 | chr15 | 645 |
| chr22:14910304-14910711 | chr22 | 407 |
| chr17:25597444-25598092 | chr17 | 648 |
| chr4:51235620-51235988 | chr4 | 368 |
| chr11:51276659-51277471 | chr11 | 812 |
| chr7:59793816-59794226 | chr7 | 410 |
| chr11:51176830-51177362 | chr11 | 532 |
| chr11:51798688-51799307 | chr11 | 619 |
| chr17:24882900-24883521 | chr17 | 621 |
| chr4:50608432-50609053 | chr4 | 621 |
| chr11:54094659-54095032 | chr11 | 373 |
| chr1:122933713-122934128 | chr1 | 415 |
| chr11:52670738-52671692 | chr11 | 954 |
| chr1:124754461-124754918 | chr1 | 457 |
| chr11:52868853-52869562 | chr11 | 709 |
| chr11:53922752-53923127 | chr11 | 375 |
| chr5:48471029-48471404 | chr5 | 375 |
| chr5:47565226-47565644 | chr5 | 418 |
| chr3:93151408-93152289 | chr3 | 881 |
| chrX:61063675-61064395 | chrX | 720 |
| chr17:23206055-23206478 | chr17 | 423 |
| chr15:19059864-19060545 | chr15 | 681 |
| chr15:19433431-19433767 | chr15 | 336 |
| chr11:52647375-52647973 | chr11 | 598 |
| chr9:44436592-44437062 | chr9 | 470 |


| 420 cenRNA:chr4:50542479-50543389 | chr4:50542479-50543389 | chr4 | 910 |
| :--- | :--- | :--- | :--- | ---: |
| 421 cenRNA:chr11:53268022-53268714 | chr11:53268022-53268714 | chr11 | 692 |
| 422 cenRNA:chr4:50948077-50949168 | chr4:50948077-50949168 | chr4 | 1091 |
| 423 cenRNA:chr1:123371606-123371991 | chr1:123371606-123371991 | chr1 | 385 |
| 424 cenRNA:chr11:54173629-54174014 | chr11:54173629-54174014 | chr11 | 385 |
| 425 cenRNA:chr11:51502875-51503351 | chr11:51502875-51503351 | chr11 | 476 |
| 426 cenRNA:chr2:92557211-92557732 | chr2:92557211-92557732 | chr2 | 521 |
| 427 cenRNA:chr11:51823244-51823811 | chr11:51823244-51823811 | chr11 | 567 |
| 428 cenRNA:chr1:123606381-123606950 | chr1:123606381-123606950 | chr1 | 569 |
| 429 cenRNA:chr11:54334500-54334934 | chr11:54334500-54334934 | chr11 | 434 |
| 430 cenRNA:chr3:92604590-92604979 | chr3:92604590-92604979 | chr3 | 389 |
| 431 cenRNA:chr11:53428821-53429980 | chr11:53428821-53429980 | chr11 | 1159 |
| 432 cenRNA:chr11:52326532-52327239 | chr11:52326532-52327239 | chr11 | 707 |

FPKM_rep1_IPCENPA_(FPKM_rep1_IPCENPA_sFPKM_rep1_IP_contr(FPKM_rep1_IP_cont

| 1442.66 | 682.546 | 1178.22 | 1338.85 |
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| 32.144 | 22.0417 | 19.2611 | 23.4381 |
| 51.2469 | 24.2789 | 48.3182 | 57.4155 |
| 8.51129 | 2.35105 | 10.4807 | 8.64865 |
| 3.72908 | 0 | 2.34643 | 0 |
| 4.79721 | 0 | 6.03832 | 15.5297 |
| 2.02234 | 0 | 1.01788 | 1.15493 |
| 1.43702 | 0.893292 | 1.44807 | 2.46457 |
| 3.33136 | 0 | 1.88812 | 2.38038 |
| 1.43677 | 1.78523 | 2.53221 | 2.4627 |
| 2.25664 | 5.60928 | 4.54646 | 0.644826 |
| 2.11917 | 0.878231 | 1.42366 | 1.21151 |
| 2.05366 | 0 | 3.10088 | 0 |
| 4.13931 | 7.71102 | 0.520831 | 3.54574 |
| 2.28051 | 2.83175 | 1.1476 | 3.90636 |
| 2.74413 | 1.13704 | 4.37759 | 5.75126 |
| 2.85736 | 1.77519 | 0.359709 | 2.44885 |
| 2.60313 | 0 | 0 | 0 |
| 6.02098 | 2.49264 | 7.07122 | 5.73093 |
| 1.75145 | 0 | 2.64517 | 2.00088 |
| 1.50482 | 0 | 2.65199 | 3.43892 |
| 1.89152 | 0 | 0.476069 | 1.08033 |
| 1.1758 | 0 | 1.7766 | 3.35967 |
| 5.42243 | 0 | 0.17076 | 1.93751 |
| 4.19155 | 0 | 4.22145 | 4.78984 |
| 1.06609 | 0 | 2.41646 | 0.609292 |
| 1.22422 | 1.52241 | 0.411316 | 0.700045 |
| 1.43677 | 0 | 1.80872 | 1.6418 |
| 1.22144 | 0 | 1.23033 | 0 |
| 2.42185 | 0 | 0 | 0 |
| 3.5029 | 0 | 1.76345 | 3.00132 |
| 4.03557 | 0 | 0.338711 | 3.07453 |
| 4.20465 | 0 | 0 | 1.20054 |
| 2.06966 | 0 | 0.520831 | 2.36383 |
| 5.81288 | 0 | 0 | 3.32115 |
| 2.85736 | 0 | 0.359709 | 0 |
| 2.82552 | 1.75543 | 2.13423 | 1.61439 |
| 2.03789 | 0 | 1.0257 | 2.3276 |
| 1.23947 | 1.54033 | 0.936356 | 0.708286 |
| 1.40493 | 0 | 0.353736 | 3.21091 |


| 1.11828 | 2.77971 | 0.844884 | 0 |
| :---: | :---: | :---: | :---: |
| 2.32869 | 0 | 3.32419 | 2.21869 |
| 2.25856 | 0 | 0.650473 | 0.553541 |
| 2.13594 | 0 | 0.537484 | 0 |
| 9.9488 | 0 | 2.50285 | 1.41992 |
| 2.31908 | 0 | 1.46004 | 1.98795 |
| 2.041 | 1.08787 | 0.881747 | 0.833722 |
| 1.90528 | 0 | 4.31575 | 5.44092 |
| 2.46508 | 0 | 1.86047 | 0 |
| 1.51376 | 0 | 0 | 0.864835 |
| 1.85131 | 0 | 0 | 1.0574 |
| 1.7052 | 2.11831 | 0 | 0 |
| 2.19957 | 0.91153 | 1.10823 | 0.838294 |
| 4.23802 | 0 | 0 | 0 |
| 5.60684 | 0 | 1.61416 | 2.74725 |
| 1.26434 | 0 | 3.50213 | 1.44497 |
| 1.51376 | 0 | 0.381105 | 0 |
| 1.03108 | 0 | 0.779062 | 0.589304 |
| 1.47858 | 1.83713 | 0.372259 | 0.844762 |
| 2.79745 | 1.98791 | 2.31618 | 2.28525 |
| 1.46125 | 0 | 0.589198 | 0.167132 |
| 1.21555 | 0 | 0.612199 | 0 |
| 1.56005 | 0 | 0.392744 | 1.78249 |
| 2.68547 | 0 | 0.676432 | 1.02334 |
| 5.3631 | 0 | 0.449974 | 1.02112 |
| 2.13594 | 0 | 0.537484 | 0 |
| 1.15954 | 0 | 0 | 0 |
| 1.47004 | 3.65303 | 3.33098 | 4.19942 |
| 1.7052 | 0 | 0.429237 | 2.92218 |
| 1.01854 | 0 | 1.28266 | 0.582143 |
| 2.70477 | 0 | 0 | 0.772739 |
| 1.68293 | 0 | 0.423637 | 0 |
| 1.54121 | 1.91484 | 0.776015 | 0.880499 |
| 1.1758 | 0 | 0 | 0 |
| 2.18788 | 0 | 0.551007 | 1.87559 |
| 1.77546 | 0 | 0.446898 | 2.02828 |
| 1.29684 | 0 | 0 | 0 |
| 1.06609 | 2.65009 | 0.805486 | 1.21858 |
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| 2.51607 | 0 | 1.26715 | 0 |
| 1.87181 | 0 | 0.471588 | 0.713445 |
| 1.20306 | 0.747926 | 1.06087 | 0.343917 |


| 1.694 | 0 | 0 | 0 |
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| 1.09076 | 0 | 0.687065 | 0.623658 |
| 1.68293 | 0 | 0.423637 | 0 |
| 1.49054 | 0 | 0.500757 | 0.28409 |
| 1.07983 | 1.34211 | 0 | 0 |
| 1.66119 | 0 | 0 | 0 |
| 1.65053 | 0 | 0 | 0 |
| 1.19819 | 0 | 0.603467 | 0 |
| 1.06532 | 0.662334 | 0.402629 | 0.609119 |
| 1.17033 | 0 | 0 | 0 |
| 1.01035 | 0 | 0 | 1.15493 |
| 2.13594 | 0 | 0 | 0 |
| 1.13341 | 4.22591 | 0.570868 | 2.59092 |
| 1.77764 | 1.10488 | 0.671649 | 1.01611 |
| 1.9731 | 1.22626 | 0.248479 | 2.81935 |
| 1.76376 | 1.46237 | 0.666725 | 0.840549 |
| 1.51376 | 0 | 0 | 0 |
| 2.37993 | 0 | 1.19755 | 1.35879 |
| 1.17033 | 0 | 0.294723 | 0 |
| 2.03789 | 0 | 1.0257 | 1.1638 |
| 1.25179 | 0 | 0 | 0 |
| 2.28631 | 2.84236 | 1.34389 | 3.04966 |
| 1.59907 | 0 | 1.20766 | 0.913511 |
| 3.98373 | 0 | 1.50385 | 0 |
| 2.64809 | 0 | 0 | 0 |
| 1.58122 | 0 | 0.53121 | 0.301366 |
| 1.43292 | 0 | 0.54148 | 0.40959 |
| 1.12328 | 0 | 0.282885 | 0 |
| 8.46794 | 7.51686 | 0.30463 | 0 |
| 2.60313 | 0 | 0 | 0 |
| 1.7169 | 0 | 0.432477 | 0 |
| 3.0764 | 0.956149 | 0.581238 | 0.439664 |
| 2.19744 | 0 | 0.276707 | 0 |
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| 1.37875 | 0.571498 | 0.463214 | 0.262791 |
| 10.0976 | 2.09068 | 1.27091 | 1.92271 |
| 1.77764 | 0 | 0 | 0 |
| 1.07521 | 1.33637 | 0.812374 | 0 |
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| 2.50357 | 0 | 1.26087 | 2.86126 |
| 2.71931 | 0 | 1.3694 | 0 |


| 3.72908 | 2.31596 | 0 | 1.06495 |
| :---: | :---: | :---: | :---: |
| 1.14372 | 0 | 0 | 1.96085 |
| 1.65053 | 0 | 0 | 0.942868 |
| 1.05712 | 0 | 0.798713 | 0 |
| 3.11454 | 0.967995 | 0.784585 | 1.33533 |
| 1.04394 | 0 | 0.788765 | 0.596644 |
| 1.32697 | 0 | 0 | 1.13796 |
| 1.20826 | 0 | 0.304505 | 0.138202 |
| 2.22665 | 0 | 0.560763 | 0.636265 |
| 1.59907 | 0 | 0 | 0.913511 |
| 1.19251 | 0 | 0 | 0 |
| 1.7877 | 0 | 0.449974 | 0 |
| 1.29684 | 0 | 0.653101 | 0.741036 |
| 1.49696 | 0 | 0.565662 | 0 |
| 2.17839 | 0 | 0.27431 | 0 |
| 3.13927 | 0 | 0 | 0 |
| 2.16899 | 0 | 0 | 0 |
| 1.73967 | 0 | 0 | 0.993722 |
| 1.25179 | 1.55561 | 0 | 0 |
| 1.71655 | 0 | 2.59253 | 1.96106 |
| 1.87608 | 0 | 0.709083 | 0 |
| 1.12832 | 0 | 1.42077 | 1.28965 |
| 2.38017 | 0 | 0.599581 | 0.90708 |
| 1.22144 | 0 | 2.46066 | 1.39599 |
| 1.79031 | 0 | 0 | 0 |
| 3.83846 | 0 | 0 | 1.09614 |
| 2.58712 | 0 | 0 | 0.49312 |
| 1.40096 | 0 | 0.352939 | 1.60184 |
| 1.02269 | 0 | 0.772725 | 0 |
| 1.66119 | 2.06372 | 0.418174 | 0.948955 |
| 1.01443 | 0 | 0.510993 | 0 |
| 2.46582 | 0 | 0.207048 | 0 |
| 1.45787 | 0 | 0.5509 | 1.25015 |
| 3.27997 | 0 | 0.412842 | 0.936855 |
| 1.29802 | 0.538046 | 0.8722 | 0.742226 |
| 1.60911 | 0 | 1.21524 | 0.919243 |
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| 2.71448 | 0 | 1.13956 | 1.55159 |
| 2.29789 | 0 | 0.578686 | 0.656602 |
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| 2.46508 | 0 | 0.620158 | 0 |
| 1.10355 | 0 | 0.277921 | 0 |


| 1.51376 | 0 | 0.762209 | 0.864835 |
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| 2.41941 | 0 | 1.21852 | 0 |
| 2.01261 | 0 | 0.253452 | 0.575154 |
| 2.67614 | 3.32545 | 0.67384 | 1.52914 |
| 1.0892 | 0 | 0.27431 | 0 |
| 1.19819 | 0 | 0 | 0.684719 |
| 2.38503 | 0 | 0 | 0 |
| 1.34283 | 0.238599 | 0.580172 | 0.438858 |
| 1.07983 | 1.34211 | 0 | 0 |
| 1.18689 | 0 | 1.19556 | 0.678267 |
| 1.694 | 2.10441 | 0 | 0 |
| 1.47858 | 0 | 0.744519 | 0.844762 |
| 1.18045 | 0 | 0 | 0 |
| 2.14126 | 0 | 0.539277 | 0.611886 |
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| 1.74701 | 1.55201 | 0.817662 | 0.428194 |
| 1.37706 | 0.570906 | 0.694101 | 1.31259 |
| 1.67199 | 0 | 0 | 0 |
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| 2.30026 | 0 | 0.38631 | 1.31497 |
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| 1.03533 | 0 | 0 | 0 |
| 1.03108 | 0 | 0.259687 | 0.589304 |
| 1.89152 | 0 | 0.952137 | 1.08033 |
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| 1.85131 | 6.89867 | 2.79578 | 1.0574 |
| 1.10032 | 0 | 0 | 1.88735 |
| 1.56963 | 0 | 0.790307 | 1.79343 |
| 3.13927 | 0 | 0.395154 | 1.79343 |
| 2.52362 | 0 | 0.423795 | 0 |
| 1.367 | 0 | 1.03259 | 0 |
| 1.367 | 0 | 1.03259 | 0 |
| 1.03889 | 0.645908 | 0.261762 | 0 |
| 1.44114 | 0 | 0 | 0.411939 |
| 1.54121 | 0 | 0 | 0 |
| 1.43509 | 0.178502 | 0.361701 | 1.14912 |


| 3.91286 | 0.608199 | 0.492961 | 0.279667 |
| :---: | :---: | :---: | :---: |
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| 3.47934 | 2.16107 | 0.437901 | 0.993722 |
| 1.20241 | 0 | 0.555577 | 0.802302 |
| 1.03533 | 0 | 0.78227 | 0.591731 |
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| 1.18199 | 0 | 0.893543 | 0.450601 |
| 1.02407 | 0 | 0.258029 | 0 |
| 2.03789 | 0 | 0.51285 | 0 |
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| 1.01035 | 0 | 0.25447 | 0 |
| 1.43677 | 0 | 1.08523 | 0 |
| 2.00699 | 0 | 0.505087 | 0 |
| 1.50242 | 0 | 0.252374 | 0.286354 |
| 1.17768 | 0.732156 | 0.890147 | 0.673332 |
| 1.37916 | 0.428793 | 0.260661 | 0.591514 |
| 1.1507 | 0 | 0.464005 | 0.13162 |
| 2.46508 | 0 | 0.620158 | 0 |
| 2.80986 | 0 | 0.353736 | 0.802728 |
| 3.68218 | 0 | 2.16356 | 0 |
| 1.08449 | 0 | 0 | 0 |
| 1.38952 | 0 | 0.69972 | 0 |
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| 1.26675 | 0 | 0.159573 | 0 |
| 1.56963 | 0 | 0 | 0.896716 |
| 1.17219 | 0 | 0.295332 | 0.335096 |
| 2.08136 | 1.29431 | 0.524536 | 1.4879 |
| 2.16172 | 0 | 0.181528 | 0.823877 |
| 1.01601 | 0.210621 | 0.341427 | 0.193699 |
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| 1.15422 | 0 | 0.29067 | 0 |
| 1.67122 | 0 | 0 | 0.477659 |
| 1.31031 | 0 | 0.329937 | 0 |
| 1.66018 | 0 | 0.836395 | 0.474505 |
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| 1.82537 | 0 | 0.918885 | 1.04261 |
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| 2.10144 | 0 | 1.23529 | 0.800919 |
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| 1.06307 | 0 | 0.267852 | 0 |
| 1.50593 | 0 | 0.189684 | 0.860892 |
| 1.90092 | 0.590949 | 0.359234 | 0 |
| 1.02268 | 0 | 0.257732 | 0 |
| 1.54196 | 0 | 0.233151 | 0.88181 |
| 1.27715 | 0 | 0.96479 | 0 |
| 1.04538 | 0 | 0 | 0 |
| 3.55092 | 0 | 0.446898 | 0 |
| 2.52869 | 0 | 0.955125 | 1.44497 |
| 1.25803 | 0 | 0 | 0 |
| 1.25803 | 1.56337 | 0 | 0.718882 |
| 1.09924 | 0 | 0.277003 | 0.419065 |
| 1.09791 | 0 | 0.138313 | 0 |
| 1.19321 | 0 | 0.100225 | 0.22744 |
| 1.94258 | 0 | 0.24464 | 0 |
| 1.45322 | 0 | 0 | 0 |
| 1.74069 | 0 | 0.219233 | 0 |
| 1.44946 | 0 | 0.365149 | 0 |
| 2.47894 | 0 | 1.24847 | 0.708286 |
| 1.73469 | 0 | 0.218477 | 0 |
| 2.17052 | 0 | 2.18469 | 3.71826 |
| 1.07983 | 0 | 0.271954 | 0 |
| 1.22739 | 0 | 0 | 0 |
| 3.68218 | 0 | 0.927241 | 2.10417 |
| 1.22739 | 0 | 1.23632 | 1.40278 |
| 3.43309 | 0 | 1.29627 | 4.90266 |
| 1.07063 | 0 | 1.07855 | 0 |
| 1.06986 | 0 | 0 | 0.305856 |
| 1.11551 | 0 | 0.0937005 | 0 |
| 1.7052 | 0 | 0 | 0 |
| 2.83139 | 0 | 0.285352 | 0.971316 |
| 1.87959 | 0 | 0.355205 | 1.07475 |
| 1.05712 | 1.3139 | 0.266238 | 1.20834 |
| 1.53351 | 0 | 0.193155 | 0 |
| 1.20392 | 0 | 0.909525 | 0.68799 |
| 1.20306 | 0 | 0.303106 | 0 |
| 1.04394 | 0 | 0.525844 | 0.596644 |
| 1.92601 | 0 | 0.728044 | 0.183571 |


| 2.38503 | 0 | 0 | 0 |
| :---: | :---: | :---: | :---: |
| 1.28292 | 0 | 0 | 0.366736 |
| 1.00006 | 0.414573 | 0.336022 | 0.190633 |
| 2.08588 | 0 | 0 | 0 |
| 1.03962 | 0 | 0.261835 | 0 |
| 3.77615 | 0 | 1.14152 | 0.431739 |
| 2.37378 | 0 | 0.896671 | 0 |
| 1.03037 | 0 | 0.64904 | 0.883714 |
| 1.02732 | 0.425872 | 0.51777 | 0.587483 |
| 1.23925 | 0 | 0.124926 | 0.283492 |
| 1.63 | 0.405431 | 0.410765 | 0.186428 |
| 1.08605 | 0 | 0.273638 | 0.931445 |
| 1.01443 | 0 | 0 | 0 |
| 1.08137 | 0 | 0.136231 | 0 |
| 1.11827 | 0 | 0.281817 | 0 |
| 1.15601 | 0 | 0.582515 | 0.991418 |
| 2.69507 | 0 | 0.452566 | 0.5135 |
| 1.24171 | 0 | 0.312839 | 0 |
| 1.14894 | 0 | 0.289343 | 0 |
| 1.33756 | 0 | 0.505464 | 0 |
| 1.33807 | 0 | 0.67384 | 0 |
| 1.33401 | 0 | 0 | 0.381333 |
| 1.14372 | 0 | 0 | 0.653618 |
| 1.33102 | 0 | 0.335147 | 0 |
| 2.27708 | 0 | 0.286725 | 1.30132 |
| 5.78116 | 0 | 0.18205 | 0 |
| 3.17828 | 0 | 0.400058 | 0.907846 |
| 2.38017 | 0 | 0.19986 | 0.45354 |
| 1.13256 | 0.704115 | 0.142676 | 0.323772 |
| 1.31714 | 3.27349 | 0.994968 | 0.752622 |
| 1.57933 | 0 | 0.397592 | 0 |
| 2.62744 | 0 | 0 | 0 |
| 1.02593 | 0.850584 | 0.430888 | 0 |
| 1.96538 | 0 | 0.247508 | 1.12333 |
| 2.23656 | 0 | 0.281628 | 0 |
| 3.1201 | 0 | 0.785488 | 0 |
| 1.55246 | 1.93001 | 0.586622 | 0 |
| 1.54239 | 0 | 0.129543 | 0.881906 |
| 2.56659 | 0 | 0.646508 | 1.46711 |
| 1.28365 | 0 | 0.646463 | 0.733504 |
| 1.92031 | 0 | 0.725511 | 0.548797 |
| 1.09394 | 1.35963 | 3.03054 | 2.50078 |


| 1.53196 | 0 | 0 | 1.75044 |
| :---: | :---: | :---: | :---: |
| 1.90528 | 0 | 0.959055 | 1.08818 |
| 1.26533 | 0 | 0.106281 | 0.964723 |
| 1.07674 | 0 | 0.678235 | 0 |
| 1.03425 | 0 | 0.0651622 | 0.295743 |
| 1.87181 | 0 | 0.314392 | 0 |
| 1.49597 | 0 | 0 | 0 |
| 1.66018 | 0 | 0.209099 | 0 |
| 1.86454 | 0 | 0.469287 | 2.12989 |
| 1.2334 | 0 | 0.621184 | 1.40964 |
| 1.34113 | 0.833718 | 0.506813 | 0.383367 |
| 3.15806 | 0 | 0.265123 | 0 |
| 1.21714 | 0 | 0.306727 | 0.174013 |
| 1.45365 | 0 | 0 | 0 |
| 1.44946 | 0 | 0.912873 | 0.414314 |
| 1.60708 | 0 | 0.404831 | 0 |
| 1.43677 | 0 | 1.08523 | 0.820899 |
| 1.78396 | 0 | 0.89871 | 0.509857 |
| 1.18199 | 0 | 0.496413 | 0.2253 |
| 1.06057 | 0 | 0.089087 | 0.202164 |
| 3.53305 | 0 | 0.445074 | 1.01 |
| 1.17493 | 0 | 0.444033 | 0.671759 |
| 1.27966 | 0.79552 | 0.161197 | 0.365802 |
| 2.34066 | 1.45448 | 0.589447 | 2.00643 |
| 1.17033 | 0 | 0.294723 | 0 |
| 1.31157 | 0 | 0.550815 | 0.499982 |
| 1.07214 | 0 | 0.135068 | 0.306508 |
| 1.04296 | 0.864704 | 0.525649 | 0.198808 |
| 1.02896 | 0.639868 | 0.388972 | 0.882688 |
| 1.29356 | 0 | 0.325953 | 0.98624 |
| 1.37916 | 0.428793 | 0.086887 | 0.197171 |
| 2.12165 | 0 | 0.400929 | 0.303274 |
| 3.44683 | 0 | 0.86803 | 0 |
| 2.86655 | 0 | 0.722457 | 1.31157 |
| 1.36734 | 0.377942 | 0.344623 | 0.260683 |
| 1.05194 | 0 | 0.132524 | 0 |
| 1.51959 | 0 | 0.191404 | 0 |
| 1.23865 | 0 | 0.156034 | 0.354086 |
| 3.39767 | 0 | 0.570703 | 1.61886 |
| 2.71931 | 0 | 0 | 0.776889 |
| 2.07778 | 0 | 0 | 0.297007 |
| 1.06207 | 0 | 0.35685 | 0.202449 |


| 1.00868 | 0.418222 | 0.33898 | 0.256414 |
| :---: | :---: | :---: | :---: |
| 2.22665 | 0 | 0 | 0 |
| 1.423 | 0 | 0.597594 | 0.271222 |
| 1.65053 | 6.15144 | 0 | 0 |
| 1.31714 | 0 | 2.98491 | 0 |
| 1.09313 | 0 | 0.275423 | 1.56254 |
| 1.63998 | 0 | 0 | 0 |
| 1.31031 | 0 | 0.329937 | 0 |
| 1.13468 | 0 | 0.357441 | 0.162227 |
| 1.12452 | 0 | 0 | 0.160775 |
| 1.02037 | 0 | 0.085711 | 0.389005 |
| 3.87064 | 0 | 0 | 0 |
| 2.13217 | 0 | 0.268495 | 0.609292 |
| 1.06158 | 0 | 0 | 0 |
| 3.81214 | 0 | 0.959934 | 0 |
| 1.44113 | 0.358464 | 0.217908 | 0.164832 |
| 1.05712 | 1.3139 | 0.266238 | 0 |
| 1.15071 | 0 | 0.144962 | 0 |
| 1.26434 | 0 | 0.318375 | 0 |
| 1.71429 | 0 | 0.287947 | 0 |
| 1.56963 | 0 | 0 | 0 |
| 1.24856 | 0 | 0.104873 | 0.475971 |
| 1.2456 | 0 | 0.62732 | 0 |
| 1.55246 | 0 | 0.586622 | 0.443737 |
| 1.22357 | 0 | 0.308271 | 0.349777 |
| 1.21764 | 0 | 0.460166 | 0 |
| 1.21764 | 0 | 0.306777 | 0 |
| 1.52281 | 1.892 | 0.766759 | 0 |
| 1.21555 | 0 | 0.3061 | 0 |
| 1.01079 | 0 | 0.339626 | 0 |
| 1.01035 | 0 | 0 | 1.15493 |
| 1.00362 | 0 | 0.126439 | 0 |
| 4.51445 | 1.86968 | 1.89428 | 1.71946 |
| 1.50482 | 0 | 0.378856 | 0 |
| 1.19819 | 0 | 0 | 1.36944 |
| 1.12049 | 0 | 0.282355 | 0.213581 |
| 1.47306 | 0 | 0.371165 | 1.4038 |
| 1.17033 | 0 | 0.589447 | 0 |
| 1.06307 | 0.660933 | 0.133926 | 0.303916 |
| 1.9477 | 0 | 0 | 1.11237 |
| 1.28951 | 0 | 0 | 0.368617 |
| 1.92031 | 0 | 0.241837 | 0 |


| 1.07418 | 0.445288 | 0.0902294 | 0.409512 |
| ---: | ---: | ---: | ---: |
| 1.55834 | 0 | 0.261762 | 0 |
| 1.13854 | 0 | 0.143462 | 0 |
| 1.42068 | 0 | 0 | 0 |
| 4.26203 | 0 | 0 | 1.62343 |
| 1.87726 | 0 | 0.47284 | 0 |
| 2.41062 | 0 | 0 | 0 |
| 1.40096 | 0 | 0.352939 | 0.800919 |
| 1.39319 | 0 | 0.350983 | 0.79648 |
| 2.22665 | 1.3837 | 0 | 0 |
| 2.77903 | 0 | 0 | 0 |
| 2.37847 | 0 | 0.466209 | 0.302275 |
| 2.5191 | 0 | 0.888621 | 0.288076 |


| FPKM_rep2_cenpa FPKM_rep2_input FPKM_rep2_mock | IPCENPA_max | FPKM_rep2_II |  |  |  |
| ---: | ---: | ---: | ---: | ---: | ---: |
| 4108.4 | 818.165 | 4680.33 | 4108.4 | 2772.63 |  |
| 167.024 | 33.7938 | 66.7278 | 167.024 | 67.4011 |  |
| 112.202 | 16.9335 | 98.4654 | 112.202 | 42.3127 |  |
| 100.647 | 15.0331 | 64.5019 | 100.647 | 41.5238 |  |
| 49.6636 | 7.00909 | 24.2729 | 49.6636 | 21.3464 |  |
| 20.8466 | 3.61158 | 11.0357 | 20.8466 | 6.00794 |  |
| 17.5938 | 2.91578 | 8.94051 | 17.5938 | 6.80277 |  |
| 14.2213 | 1.61278 | 5.3192 | 14.2213 | 5.73374 |  |
| 13.3581 | 1.22914 | 5.20249 | 13.3581 | 5.4689 |  |
| 11.8747 | 1.61453 | 3.83711 | 11.8747 | 3.86757 |  |
| 11.1449 | 3.43898 | 6.14374 | 11.1449 | 6.66885 |  |
| 10.5868 | 0.643181 | 5.56844 | 10.5868 | 3.05577 |  |
| 10.5828 | 2.17515 | 4.41731 | 10.5828 | 4.55652 |  |
| 10.3681 | 0.935842 | 6.75183 | 10.3681 | 3.44052 |  |
| 9.32917 | 1.41468 | 2.72173 | 9.32917 | 4.0007 |  |
| 8.6335 | 0.519518 | 3.74818 | 8.6335 | 5.2891 |  |
| 8.25386 | 1.77312 | 4.81603 | 8.25386 | 3.42158 |  |
| 7.98949 | 2.4426 | 11.2785 | 7.98949 | 2.76306 |  |
| 7.97587 | 0 | 0.855484 | 7.97587 | 0.335329 |  |
| 7.59961 | 1.60057 | 3.29932 | 7.59961 | 6.20761 |  |
| 7.58089 | 0.199578 | 1.15192 | 7.58089 | 1.12881 |  |
| 7.32898 | 1.02904 | 8.41417 | 7.32898 | 2.1341 |  |
| 7.163 | 0.215516 | 1.24391 | 7.163 | 2.19411 |  |
| 6.78881 | 0.67022 | 2.70785 | 6.78881 | 2.27445 |  |
| 6.6067 | 1.54605 | 2.45395 | 6.6067 | 1.92378 |  |
| 6.5533 | 0.637015 | 5.51506 | 6.5533 | 1.80147 |  |
| 6.54066 | 1.21547 | 4.20927 | 6.54066 | 1.92492 |  |
| 6.48343 | 1.07066 | 1.61208 | 6.48343 | 1.94834 |  |
| 6.47958 | 1.47385 | 8.03412 | 6.47958 | 1.48197 |  |
| 6.17058 | 1.25318 | 4.82205 | 6.17058 | 2.67768 |  |
| 6.11177 | 0 | 0.796015 | 6.11177 | 0.312018 |  |
| 6.00154 | 0.997889 | 15.5509 | 6.00154 | 3.38642 |  |
| 5.82434 | 1.22667 | 1.32752 | 5.82434 | 4.50973 |  |
| 5.68572 | 0.239496 | 1.38231 | 5.68572 | 0.81275 |  |
| 5.5975 | 0 | 2.72173 | 5.5975 | 3.46727 |  |
| 5.50509 | 0.165634 | 0.478 | 5.81288 | 0.749457 |  |
| 5.41224 | 0.32568 | 1.40981 | 5.41224 | 1.47363 |  |
| 5.352 | 0.483082 | 3.25295 | 5.352 | 1.27508 |  |
| 5.143447 | 0.282591 | 2.44658 | 5.14344 | 2.36363 |  |
| 5.06892 | 0.320272 | 2.31067 | 5.06892 | 1.81145 |  |
|  |  |  |  |  |  |


| 5.04454 | 1.6574 | 3.31136 | 5.04454 | 2.74016 |
| :---: | :---: | :---: | :---: | :---: |
| 5.04365 | 0.97373 | 3.321 | 5.04365 | 2.00269 |
| 5.01007 | 0.846597 | 2.44318 | 5.01007 | 1.41568 |
| 5.00627 | 0.243318 | 1.40438 | 5.00627 | 1.3762 |
| 4.93143 | 0 | 0 | 9.9488 | 0.961265 |
| 4.81204 | 0.264384 | 0.381491 | 4.81204 | 2.09349 |
| 4.58023 | 0.69854 | 3.55184 | 4.58023 | 2.52107 |
| 4.46645 | 1.73665 | 12.5294 | 4.46645 | 9.33135 |
| 4.44332 | 0.280745 | 1.62039 | 4.44332 | 0.952732 |
| 4.36888 | 0 | 2.48945 | 4.36888 | 0.975802 |
| 4.34011 | 0.843763 | 1.82625 | 4.34011 | 1.43169 |
| 4.30557 | 1.16589 | 1.12154 | 4.30557 | 0.219808 |
| 4.23481 | 0.668924 | 3.61957 | 4.23481 | 2.08088 |
| 4.20257 | 0 | 0 | 4.23802 | 1.36532 |
| 4.19239 | 0.639389 | 1.5816 | 5.60684 | 2.78977 |
| 4.10599 | 0.864768 | 5.82312 | 4.10599 | 0.489111 |
| 4.09583 | 0.172526 | 2.98734 | 4.09583 | 0.390321 |
| 4.09335 | 0.35268 | 3.05339 | 4.09335 | 1.06387 |
| 4.00076 | 0.505564 | 2.918 | 4.00076 | 1.71568 |
| 3.96838 | 0.410295 | 1.57875 | 3.96838 | 2.32062 |
| 3.95766 | 0.400094 | 2.50169 | 3.95766 | 1.43319 |
| 3.94767 | 1.10857 | 1.5996 | 3.94767 | 0.940506 |
| 3.93952 | 0.355589 | 1.02619 | 3.93952 | 0.201121 |
| 3.87722 | 0.204147 | 1.76743 | 3.87722 | 1.27011 |
| 3.86879 | 0.407405 | 0.587863 | 5.3631 | 0.460856 |
| 3.85098 | 0.486636 | 1.40438 | 3.85098 | 0.550481 |
| 3.76595 | 0.396576 | 0.381491 | 3.76595 | 0.747676 |
| 3.71248 | 1.34038 | 2.41762 | 3.71248 | 2.46389 |
| 3.69049 | 0.38863 | 1.12154 | 3.69049 | 1.75847 |
| 3.67601 | 0.232263 | 0.670285 | 3.67601 | 0.131368 |
| 3.65966 | 1.23323 | 0.444869 | 3.65966 | 0.174378 |
| 3.64235 | 0.19178 | 0 | 3.64235 | 0.433882 |
| 3.61401 | 0.175651 | 0.506908 | 3.61401 | 0.198695 |
| 3.60656 | 0.402132 | 0.773671 | 3.60656 | 1.06141 |
| 3.55308 | 0.623601 | 2.15957 | 3.55308 | 1.693 |
| 3.52214 | 0 | 1.75153 | 3.52214 | 0.228853 |
| 3.50952 | 0.739145 | 2.98632 | 3.50952 | 0.334447 |
| 3.4627 | 0.48619 | 2.80618 | 3.4627 | 1.64993 |
| 3.41033 | 0.269345 | 1.94325 | 3.41033 | 0.304682 |
| 3.4046 | 0.14341 | 1.24159 | 3.4046 | 1.13557 |
| 3.37885 | 0.355812 | 1.43757 | 3.37885 | 1.20748 |
| 3.36614 | 0.68608 | 1.58396 | 3.36614 | 1.31935 |


| 3.36075 | 0.19304 | 0 | 3.36075 | 0.436732 |
| ---: | ---: | ---: | ---: | ---: |
| 3.34744 | 0.55986 | 2.15426 | 3.34744 | 1.05552 |
| 3.33882 | 0.19178 | 0.553456 | 3.33882 | 0.433882 |
| 3.31875 | 0.170019 | 0.981311 | 3.31875 | 1.15395 |
| 3.31246 | 0.123113 | 0.355291 | 3.31246 | 0.417796 |
| 3.29576 | 0.378613 | 1.09264 | 3.29576 | 1.28486 |
| 3.27462 | 0 | 0 | 3.27462 | 0 |
| 3.2428 | 0.273189 | 0 | 3.2428 | 0.463545 |
| 3.17324 | 0.546809 | 1.40269 | 3.17324 | 1.16837 |
| 3.16747 | 0.800526 | 1.54015 | 3.16747 | 0.603701 |
| 3.0995 | 0.345595 | 1.66225 | 3.0995 | 1.82437 |
| 3.08078 | 0.243318 | 1.40438 | 3.08078 | 0.275241 |
| 3.06763 | 0.258431 | 0.745803 | 4.22591 | 0.584673 |
| 3.04776 | 0.405406 | 1.46245 | 3.04776 | 1.49043 |
| 3.02653 | 0.449945 | 0 | 3.02653 | 2.67213 |
| 3.02542 | 0.670724 | 2.32276 | 3.02542 | 1.97267 |
| 3.00361 | 0 | 0.497889 | 3.00361 | 0.19516 |
| 3.00308 | 0 | 3.12904 | 3.00308 | 0.613254 |
| 2.9563 | 0.533684 | 0.770075 | 2.9563 | 0.754626 |
| 2.93959 | 0 | 0 | 2.93959 | 0.262626 |
| 2.93601 | 0.142698 | 0.823621 | 2.93601 | 1.45278 |
| 2.88862 | 0.260732 | 0.752444 | 2.88862 | 1.37639 |
| 2.88424 | 0.91118 | 1.05182 | 2.88424 | 0.618434 |
| 2.8733 | 0.226931 | 1.30979 | 3.98373 | 2.05363 |
| 2.86644 | 0.301853 | 2.17778 | 2.86644 | 0.853638 |
| 2.85452 | 0.300597 | 1.90848 | 2.85452 | 1.42815 |
| 2.84505 | 0.490254 | 0.707409 | 2.84505 | 0.369716 |
| 2.83756 | 0.128062 | 0.739144 | 2.83756 | 0.144863 |
| 2.83741 | 0 | 0 | 8.46794 | 0 |
| 2.81501 | 0.889312 | 0 | 2.81501 | 4.02394 |
| 2.78876 | 0.195782 | 3.67253 | 2.78876 | 0.442935 |
| 2.77631 | 0.175417 | 0.253117 | 3.0764 | 0.992155 |
| 2.77558 | 0.375795 | 0.723001 | 2.77558 | 0.566797 |
| 2.77255 | 0 | 0.919177 | 2.77255 | 0.720589 |
| 2.75399 | 0.711846 | 3.13853 | 2.75399 | 1.23022 |
| 2.73805 | 0.524241 | 1.66419 | 2.73805 | 1.06743 |
| 2.73176 | 1.15068 | 2.76728 | 10.0976 | 2.60329 |
| 2.72694 | 0.506758 | 1.16996 | 2.72694 | 0.229297 |
| 2.71624 | 0.122587 | 1.41509 | 2.71624 | 1.3867 |
| 2.71026 | 0.321081 | 1.54434 | 7.50906 | 1.9371 |
| 2.71017 | 0.428094 | 0.71017 | 0.484259 |  |
| 2.69817 | 0.464944 | 3.57807 | 2.71931 | 0.175314 |
|  |  |  |  | 0 |


|  |  |  |  |  |
| ---: | ---: | ---: | ---: | ---: |
| 2.68989 | 0.424891 | 2.45238 | 3.72908 | 1.92254 |
| 2.68278 | 0.39117 | 1.12887 | 2.68278 | 0.884981 |
| 2.67923 | 0 | 1.08563 | 2.67923 | 0 |
| 2.67057 | 0.361577 | 0 | 2.67057 | 0.954366 |
| 2.67017 | 0.443976 | 1.02501 | 3.11454 | 0.301334 |
| 2.63731 | 0.238049 | 2.06094 | 2.63731 | 1.3464 |
| 2.63478 | 0.378352 | 1.52863 | 2.63478 | 1.36957 |
| 2.61808 | 0.248129 | 1.27301 | 2.61808 | 0.686112 |
| 2.61155 | 0 | 0.366301 | 2.61155 | 0.143581 |
| 2.59581 | 0 | 0.525912 | 2.59581 | 0.412289 |
| 2.58196 | 0.271896 | 0.78466 | 2.58196 | 0.461351 |
| 2.57919 | 0.407405 | 1.17573 | 2.57919 | 1.61299 |
| 2.57365 | 0.295658 | 2.55971 | 2.57365 | 0.836118 |
| 2.56682 | 0.170716 | 0.246334 | 2.56682 | 0.772455 |
| 2.555 | 0.49672 | 3.22532 | 2.555 | 0.561888 |
| 2.54809 | 0.178886 | 2.06497 | 3.13927 | 0.809419 |
| 2.54398 | 0.123644 | 0 | 2.54398 | 0.279732 |
| 2.50999 | 0.198237 | 0.57209 | 2.50999 | 0.448491 |
| 2.48432 | 0.998886 | 1.23543 | 2.48432 | 0.807098 |
| 2.47667 | 0.195606 | 2.25799 | 2.47667 | 1.99142 |
| 2.45556 | 0.535002 | 1.08077 | 2.45556 | 0.968308 |
| 2.4431 | 0.514545 | 0 | 2.4431 | 0.145513 |
| 2.43434 | 0.633335 | 3.65547 | 2.43434 | 1.5352 |
| 2.42416 | 0.556969 | 1.20551 | 2.42416 | 1.41759 |
| 2.42326 | 0.102073 | 1.17829 | 2.42326 | 0.577325 |
| 2.42259 | 0.874673 | 1.2621 | 3.83846 | 1.48414 |
| 2.41324 | 0.0983723 | 0.567783 | 2.58712 | 0.0556392 |
| 2.40231 | 0.239663 | 0.922186 | 2.40231 | 0.361474 |
| 2.39912 | 0.233208 | 3.36505 | 2.39912 | 1.31902 |
| 2.39692 | 0.56792 | 2.18527 | 2.39692 | 1.71314 |
| 2.37977 | 0.231326 | 1.33516 | 2.37977 | 1.30838 |
| 2.37354 | 0.0937303 | 0.811485 | 2.46582 | 0.530137 |
| 2.36826 | 0.0831306 | 0.959622 | 2.36826 | 0.564222 |
| 2.36635 | 0.373786 | 2.15741 | 3.27997 | 0.422825 |
| 2.34344 | 0.246778 | 1.28191 | 2.34344 | 0.837462 |
| 2.32187 | 0.366759 | 2.11685 | 2.32187 | 1.45207 |
| 2.28906 | 0.361577 | 0 | 2.28906 | 0.272676 |
| 2.28613 | 0.103175 | 0.595505 | 2.71448 | 0.116712 |
| 2.2804 | 0.523941 | 3.02407 | 2.29789 | 0.59268 |
| 2.25679 | 0.814811 | 1.17573 | 2.25679 | 1.15214 |
| 2.22166 | 0.842234 | 3.24079 | 2.46508 | 1.58789 |
| 2.19038 | 0.629073 | 0 | 2.19038 | 0.711605 |
|  |  |  |  |  |
|  | 0 |  |  |  |


| 2.18444 | 0.172526 | 0 | 2.18444 | 0.390321 |
| :---: | :---: | :---: | :---: | :---: |
| 2.18263 | 0.275812 | 2.38788 | 2.41941 | 0.935991 |
| 2.17912 | 0.229474 | 0.662237 | 2.17912 | 1.42769 |
| 2.17258 | 0.762617 | 0.88033 | 3.32545 | 2.24294 |
| 2.16193 | 0.12418 | 1.07511 | 2.16193 | 0.702359 |
| 2.16187 | 0.136594 | 0.394196 | 2.16187 | 0.61806 |
| 2.15164 | 0.135948 | 0.78466 | 2.38503 | 0.615135 |
| 2.1477 | 0.28453 | 2.02122 | 2.1477 | 0.544685 |
| 2.14336 | 0.123113 | 1.06587 | 2.14336 | 0.278531 |
| 2.1415 | 0.676536 | 0.780963 | 2.1415 | 0.306118 |
| 2.13866 | 0.19304 | 2.22836 | 2.13866 | 0.655097 |
| 2.13374 | 0 | 0.486333 | 2.13374 | 0.571892 |
| 2.13091 | 0.0673191 | 0.194275 | 2.13091 | 0.533058 |
| 2.12511 | 0.122065 | 0.352266 | 2.14126 | 0.828477 |
| 2.1247 | 0.38356 | 1.66037 | 2.1247 | 1.73553 |
| 2.11804 | 0.484048 | 2.5473 | 2.11804 | 0.805226 |
| 2.11357 | 0.261849 | 1.20907 | 2.11357 | 1.18481 |
| 2.11092 | 0.571607 | 0.549865 | 2.11092 | 0.6466 |
| 2.08952 | 0.240042 | 1.0391 | 2.08952 | 0.135767 |
| 2.07588 | 0.437205 | 0.50469 | 2.30026 | 0.494565 |
| 2.07309 | 0.261971 | 3.02407 | 2.07309 | 0.74085 |
| 2.07296 | 0 | 0 | 4.5996 | 0.29632 |
| 2.07056 | 0.373786 | 1.61805 | 2.07056 | 0.422825 |
| 2.06932 | 0.577717 | 1.31623 | 2.13214 | 1.5134 |
| 2.06367 | 0 | 2.25775 | 2.06367 | 0.44249 |
| 2.06333 | 0.434561 | 2.09016 | 2.54143 | 1.31086 |
| 2.06144 | 0.217081 | 1.25294 | 2.06144 | 0.982247 |
| 2.0551 | 0 | 1.02199 | 2.0551 | 0.267062 |
| 2.04668 | 0.35268 | 0 | 2.04668 | 0.265967 |
| 2.04657 | 0 | 3.10977 | 2.04657 | 0.975162 |
| 2.01748 | 0.364205 | 1.83934 | 2.01748 | 0.617981 |
| 2.00313 | 0.421881 | 1.82625 | 6.89867 | 1.43169 |
| 1.98632 | 0 | 0 | 1.98632 | 0.070984 |
| 1.98185 | 0 | 0 | 1.98185 | 0.809419 |
| 1.98185 | 0.536657 | 0.516243 | 3.13927 | 1.21413 |
| 1.97367 | 0.0959257 | 0 | 2.52362 | 0.217022 |
| 1.97289 | 0 | 0 | 1.97289 | 0.528782 |
| 1.97289 | 0.467454 | 0.449673 | 1.97289 | 0.705043 |
| 1.96926 | 0.0592497 | 0.512964 | 1.96926 | 0.402139 |
| 1.95093 | 0 | 1.66008 | 1.95093 | 0.371835 |
| 1.94601 | 0.175651 | 0.506908 | 1.94601 | 0 |
| 1.94364 | 0.261986 | 0.614301 | 1.94364 | 0.518627 |


|  |  |  |  |  |
| ---: | ---: | ---: | ---: | ---: |
| 1.94259 | 0.278953 | 1.28804 | 3.91286 | 0.378661 |
| 1.89956 | 0 | 0.346367 | 1.89956 | 0.271535 |
| 1.89522 | 0.399156 | 0.575959 | 1.89522 | 0.225762 |
| 1.89417 | 0.2992 | 1.72691 | 2.62744 | 0.338454 |
| 1.88249 | 0.198237 | 1.71627 | 3.47934 | 0.224245 |
| 1.88174 | 0.320102 | 0.725826 | 1.88174 | 1.0087 |
| 1.86828 | 0.354133 | 1.02199 | 1.86828 | 1.06825 |
| 1.85016 | 0.467598 | 0.224906 | 2.05 | 0.528946 |
| 1.84949 | 0.26967 | 2.20501 | 1.84949 | 1.27104 |
| 1.84874 | 0.11681 | 1.3484 | 1.84874 | 0.462471 |
| 1.83724 | 0 | 0.670006 | 2.03789 | 1.0505 |
| 1.82361 | 0.192037 | 1.66259 | 2.24487 | 1.23098 |
| 1.82323 | 0 | 0.664898 | 1.82323 | 1.30312 |
| 1.81428 | 0.327522 | 0.472595 | 1.81428 | 2.0377 |
| 1.80943 | 0.457304 | 0 | 2.00699 | 1.81055 |
| 1.80822 | 0.399873 | 0.329711 | 1.80822 | 0.581573 |
| 1.80703 | 0.268646 | 0.775281 | 1.80703 | 0.8357 |
| 1.80534 | 0.196668 | 0.908099 | 1.80534 | 0.800893 |
| 1.78693 | 0.446366 | 1.66703 | 1.78693 | 0.504928 |
| 1.77733 | 0.561489 | 3.24079 | 2.46508 | 0.952732 |
| 1.77412 | 0.160136 | 0 | 2.80986 | 0.36229 |
| 1.77161 | 2.65848 | 6.8645 | 3.68218 | 1.89933 |
| 1.76122 | 0.123644 | 0.356824 | 1.76122 | 0.419598 |
| 1.75468 | 0.475143 | 3.65656 | 1.75468 | 0.895801 |
| 1.75416 | 0.277084 | 0.999542 | 1.82204 | 0.626873 |
| 1.75366 | 0.246227 | 1.42116 | 1.75366 | 1.67118 |
| 1.74315 | 0.220276 | 1.27139 | 2.40133 | 0.498352 |
| 1.73626 | 0.235077 | 1.58295 | 2.06122 | 0.709116 |
| 1.7272 | 0.181884 | 0.699862 | 1.7272 | 0.274329 |
| 1.72615 | 0.256622 | 0.370291 | 2.2499 | 0.58058 |
| 1.71497 | 0.0722383 | 1.66777 | 1.71497 | 0.408579 |
| 1.69872 | 0.357771 | 3.09746 | 1.69872 | 0.202355 |
| 1.6928 | 0.267393 | 2.50791 | 1.6928 | 0.680566 |
| 1.6912 | 0.207775 | 0.513955 | 2.08136 | 0.436492 |
| 1.6908 | 0.493065 | 1.18577 | 2.16172 | 1.30142 |
| 1.68181 | 0.328447 | 1.17089 | 1.68181 | 1.02719 |
| 1.66772 | 0 | 0.33788 | 1.66772 | 0.264881 |
| 1.66608 | 0.131586 | 8.73407 | 1.66608 | 1.04195 |
| 1.65893 | 0.190576 | 0.824971 | 1.67122 | 0.431158 |
| 1.65476 | 0 | 0 | 1.65476 | 0.506873 |
| 1.64797 | 0.189318 | 1.36587 | 1.66018 | 0.749544 |
| 1.64591 | 0 | 1.82537 | 0.70583 |  |
|  |  |  |  |  |


| 1.64591 | 0.207989 | 1.8007 | 1.82537 | 0 |
| :---: | :---: | :---: | :---: | :---: |
| 1.64369 | 0.31955 | 2.07492 | 2.10144 | 0.813317 |
| 1.63434 | 0.344212 | 0.662237 | 1.63434 | 0.648951 |
| 1.6332 | 0.217244 | 1.56735 | 2.38065 | 0.614364 |
| 1.63124 | 0.121256 | 0.699862 | 1.63124 | 0.480075 |
| 1.63086 | 0.257609 | 0.49562 | 1.63086 | 0.485677 |
| 1.63011 | 0.108417 | 0.469317 | 1.90092 | 0.490562 |
| 1.61578 | 0.204181 | 0.757598 | 1.61578 | 0.659911 |
| 1.6148 | 0.246277 | 1.21839 | 1.6148 | 0.596973 |
| 1.61293 | 0.436759 | 1.26044 | 1.61293 | 0.658747 |
| 1.60411 | 0.238478 | 0.516164 | 1.60411 | 0.472089 |
| 1.60097 | 0.20231 | 4.67075 | 3.55092 | 1.14426 |
| 1.59677 | 0.144128 | 1.24781 | 2.52869 | 0.815185 |
| 1.58881 | 0.286819 | 0.413864 | 1.58881 | 0.648897 |
| 1.58881 | 0 | 0.413864 | 1.58881 | 0.648897 |
| 1.58774 | 0.167198 | 0.723774 | 1.58774 | 0.614687 |
| 1.58559 | 0 | 0.361395 | 1.58559 | 0.424974 |
| 1.57981 | 0.317603 | 0.916566 | 1.57981 | 0.307947 |
| 1.57752 | 0 | 0 | 1.94258 | 0.751667 |
| 1.57288 | 0.165634 | 0.956 | 1.57288 | 0.374728 |
| 1.57077 | 0.198493 | 1.14566 | 1.74069 | 0.673603 |
| 1.56974 | 0.0826513 | 0.238522 | 1.56974 | 0.373979 |
| 1.56539 | 0.141296 | 2.03882 | 2.47894 | 2.07783 |
| 1.56535 | 0.0989041 | 0.856278 | 1.73469 | 0.783159 |
| 1.56529 | 1.23626 | 0 | 2.17052 | 0 |
| 1.55881 | 0.246227 | 0 | 1.55881 | 0.417796 |
| 1.55016 | 0.699601 | 0 | 1.55016 | 0.633109 |
| 1.55016 | 0.13992 | 0.807588 | 3.68218 | 1.89933 |
| 1.55016 | 0.13992 | 1.21138 | 1.55016 | 1.4245 |
| 1.54792 | 0 | 0 | 3.43309 | 1.10634 |
| 1.54553 | 0.48826 | 0 | 1.54553 | 0.690398 |
| 1.54509 | 0.12203 | 1.0565 | 1.54509 | 0.3451 |
| 1.5441 | 0.0424181 | 0.489655 | 1.5441 | 0.191933 |
| 1.5377 | 0 | 1.12154 | 1.7052 | 0.439617 |
| 1.53337 | 0.452124 | 0.745588 | 2.83139 | 0.584504 |
| 1.52699 | 0.268001 | 0.773421 | 1.87959 | 0.606324 |
| 1.52604 | 0.241051 | 3.13041 | 1.52604 | 0.818028 |
| 1.52231 | 0.087441 | 0.252345 | 1.53351 | 0.197826 |
| 1.52054 | 0.411741 | 0 | 1.52054 | 0.310507 |
| 1.52019 | 0.137216 | 0.791979 | 1.52019 | 0.232827 |
| 1.50703 | 0.238049 | 0 | 1.50703 | 0.40392 |
| 1.50693 | 0.329584 | 0.951143 | 1.92601 | 0.207125 |


| 1.50615 | 0.271896 | 1.17699 | 2.38503 | 0.615135 |
| ---: | ---: | ---: | ---: | ---: |
| 1.50527 | 0.07316 | 0.211132 | 1.50527 | 0.413792 |
| 1.50471 | 0.152117 | 0.329244 | 1.50471 | 0.774333 |
| 1.50435 | 0 | 0.685758 | 2.08588 | 0.5376 |
| 1.5008 | 0.237064 | 0.342071 | 1.5008 | 0.536333 |
| 1.49945 | 0 | 1.24277 | 3.77615 | 1.0717 |
| 1.49905 | 0.135307 | 0 | 2.37378 | 0.459177 |
| 1.48808 | 0.411348 | 1.01752 | 1.48808 | 1.59537 |
| 1.48389 | 0.117197 | 0.338217 | 1.48389 | 0.309336 |
| 1.47687 | 0.0565537 | 0.408019 | 1.47687 | 0.351853 |
| 1.47153 | 0.334715 | 0.321983 | 1.63 | 0.925536 |
| 1.47043 | 0 | 0.178746 | 1.47043 | 0.770703 |
| 1.46447 | 0.115663 | 1.33516 | 1.46447 | 0.261675 |
| 1.4641 | 0.0616714 | 0.53393 | 1.4641 | 0.139525 |
| 1.4639 | 0.127578 | 0.552265 | 1.4639 | 0.613343 |
| 1.46077 | 0.263704 | 1.14153 | 1.46077 | 0.14915 |
| 1.45915 | 0.102438 | 0.295625 | 2.69507 | 0.46351 |
| 1.45693 | 0 | 0.817409 | 1.45693 | 0.0801011 |
| 1.45117 | 0.261971 | 1.13403 | 1.45117 | 0.59268 |
| 1.44863 | 0 | 0.440238 | 1.44863 | 0.258844 |
| 1.44839 | 0.152523 | 1.3205 | 1.44839 | 0.345068 |
| 1.44478 | 0.0760719 | 0.658605 | 1.44478 | 0.430262 |
| 1.44457 | 0.26078 | 1.50516 | 1.44457 | 0.737484 |
| 1.44076 | 1.06205 | 0.875698 | 1.44076 | 0.686504 |
| 1.43804 | 0.2596 | 0 | 2.27708 | 0.587318 |
| 1.43479 | 0.164827 | 1.90269 | 5.78116 | 1.11871 |
| 1.43318 | 0.362212 | 1.0453 | 3.17828 | 0.819466 |
| 1.43196 | 0.0904765 | 0.52221 | 2.38017 | 1.33051 |
| 1.43115 | 0.193767 | 0.186397 | 1.43115 | 0.219189 |
| 1.42576 | 0.300281 | 1.29986 | 3.27349 | 1.18887 |
| 1.42434 | 0 | 1.55829 | 1.57933 | 1.42522 |
| 1.42062 | 0.5984 | 1.72691 | 2.62744 | 0.676908 |
| 1.42013 | 0.0780249 | 1.01327 | 1.42013 | 0.485438 |
| 1.41868 | 0.112047 | 0.646708 | 1.96538 | 0.126747 |
| 1.41247 | 0 | 1.10379 | 2.23656 | 0.288438 |
| 1.40697 | 0.177795 | 0.513095 | 3.1201 | 1.20672 |
| 1.40101 | 0.177042 | 0.510923 | 1.93001 | 0.400538 |
| 1.39223 | 0.46915 | 0.169239 | 1.54239 | 0.26535 |
| 1.38964 | 0.487789 | 2.53387 | 2.56659 | 0.551785 |
| 1.38954 | 0.11141 | 1.38954 | 0.165524 |  |
| 1.38618 | 0.34944 | 1.07978 | 1.38176 | 0.495371 |
| 1.38176 |  |  | 0.141083 |  |
|  | 0 |  |  |  |
|  | 0 |  |  |  |


|  |  |  | 1.18502 |  |
| ---: | ---: | ---: | ---: | ---: | ---: |
| 1.38167 | 0.349194 | 3.52707 | 1.53196 | 0.491124 |
| 1.37429 | 0 | 1.25294 | 1.90528 | 0.380977 |
| 1.37067 | 0.240565 | 0.694244 | 1.37067 |  |
| 1.36064 | 0.122814 | 1.59493 | 1.36064 | 1.11142 |
| 1.35394 | 0.0884966 | 0.766173 | 1.35394 | 0.567273 |
| 1.35154 | 0.142325 | 1.8483 | 1.87181 | 0.482992 |
| 1.34925 | 0.170501 | 0 | 1.49597 | 0.38574 |
| 1.34834 | 0 | 1.0927 | 1.66018 | 0.428311 |
| 1.34494 | 0.212446 | 0.613094 | 1.86454 | 0.480635 |
| 1.3352 | 0.281209 | 2.84038 | 1.3352 | 0.318103 |
| 1.33145 | 0.305911 | 0.882825 | 1.34113 | 0.519069 |
| 1.32969 | 0.840147 | 1.73183 | 3.15806 | 0.407302 |
| 1.31859 | 0.242997 | 1.10198 | 1.31859 | 0.903167 |
| 1.3119 | 0.165781 | 0.478424 | 1.45365 | 0.281296 |
| 1.30812 | 0.330605 | 0.715567 | 1.44946 | 0.560969 |
| 1.30525 | 0.0916332 | 0.528886 | 1.60708 | 0.20731 |
| 1.29592 | 0.163761 | 0.472595 | 1.43677 | 0.555737 |
| 1.28782 | 0.406845 | 1.76116 | 1.78396 | 1.38066 |
| 1.28042 | 0.0898901 | 0.389119 | 1.28042 | 0.406734 |
| 1.27659 | 0.322637 | 0.814706 | 1.27659 | 0.364966 |
| 1.27555 | 0.201484 | 0.19382 | 3.53305 | 1.51946 |
| 1.27257 | 0.134009 | 2.32041 | 1.27257 | 1.13693 |
| 1.27045 | 0.0729738 | 0.631782 | 1.27966 | 0.412739 |
| 1.26699 | 0.133421 | 0 | 2.34066 | 0.603701 |
| 1.26699 | 0.133421 | 0 | 1.26699 | 0.452776 |
| 1.26288 | 0.598448 | 0.287842 | 1.31157 | 0.789789 |
| 1.25806 | 0.183436 | 0.529375 | 1.25806 | 0.276669 |
| 1.25539 | 0.15864 | 0.801182 | 1.25539 | 0.583224 |
| 1.25411 | 0.293479 | 1.01634 | 1.25411 | 0.730361 |
| 1.24554 | 0.147558 | 1.41946 | 1.29356 | 0.278196 |
| 1.24506 | 0.0786672 | 1.02161 | 1.37916 | 0.489435 |
| 1.24479 | 0.3025 | 0.698386 | 2.12165 | 0.752812 |
| 1.24386 | 0.261971 | 1.13403 | 3.44683 | 0.29634 |
| 1.24231 | 0.305252 | 0.943845 | 2.86655 | 0.813921 |
| 1.23458 | 0.277352 | 1.10056 | 1.36734 | 0.705914 |
| 1.23437 | 0.179981 | 1.38508 | 1.23437 | 0.475052 |
| 1.23424 | 0.259944 | 0.500113 | 1.51959 | 0.196032 |
| 1.22975 | 0.141273 | 0.611546 | 1.23865 | 0.319615 |
| 1.2267 | 0.258357 | 1.49118 | 3.39767 | 0.365315 |
| 1.22644 | 0.0592497 | 0.341976 | 2.07778 | 0.525943 |
| 1.21906 | 0.282705 | 0.932405 | 1.21447 | 0.134046 |
| 1.21447 |  |  | 0.54822 |  |
|  | 0 |  |  |  |


| 1.21437 | 0.153456 | 0.774998 | 1.21437 | 0.448437 |
| :---: | :---: | :---: | :---: | :---: |
| 1.20533 | 0.253857 | 0.732602 | 2.22665 | 0.430743 |
| 1.19886 | 0.054106 | 0.624575 | 1.423 | 0.489636 |
| 1.19077 | 0.564277 | 0 | 6.15144 | 0.851078 |
| 1.18813 | 0 | 0.433288 | 1.31714 | 0.849191 |
| 1.18402 | 0.187026 | 0.359823 | 1.18402 | 0.423126 |
| 1.18318 | 0 | 1.61805 | 1.63998 | 0.211413 |
| 1.18197 | 0.149362 | 0.431042 | 1.31031 | 0.337916 |
| 1.17806 | 0.0970878 | 0.373579 | 1.17806 | 0.512519 |
| 1.16752 | 0.0641459 | 0.462795 | 1.16752 | 0.507932 |
| 1.1668 | 0.155205 | 1.00778 | 1.1668 | 0.614486 |
| 1.16386 | 0 | 0 | 3.87064 | 0 |
| 1.15423 | 0.48619 | 1.05232 | 2.13217 | 0.549976 |
| 1.14936 | 0.484137 | 0.698583 | 1.14936 | 0.273827 |
| 1.14629 | 0.144854 | 0 | 3.81214 | 0.491574 |
| 1.14494 | 0.197294 | 0.569367 | 1.44113 | 1.0415 |
| 1.14453 | 0.241051 | 0.695646 | 1.3139 | 0.545352 |
| 1.14249 | 0.0656241 | 0.757535 | 1.15071 | 0.742337 |
| 1.14055 | 0 | 0 | 1.26434 | 0.815185 |
| 1.1347 | 0.130353 | 0.752368 | 1.71429 | 0.221182 |
| 1.13248 | 0 | 1.03249 | 1.56963 | 1.01177 |
| 1.12709 | 0.0949513 | 1.37009 | 1.24856 | 0.537043 |
| 1.12366 | 0.283987 | 0.819554 | 1.2456 | 0 |
| 1.12081 | 0.265563 | 0 | 1.55246 | 0.600808 |
| 1.10435 | 0.139554 | 0.805472 | 1.22357 | 0.789313 |
| 1.099 | 0.0694388 | 0 | 1.21764 | 0.628392 |
| 1.099 | 0.138878 | 0.80157 | 1.21764 | 0.471294 |
| 1.09874 | 0 | 1.50258 | 1.892 | 1.37428 |
| 1.09658 | 0.277142 | 0.7998 | 1.21555 | 0.313502 |
| 1.09501 | 0.0768742 | 1.22018 | 1.09501 | 0.26088 |
| 1.09394 | 0.115198 | 1.99469 | 1.09394 | 0.781871 |
| 1.0871 | 0 | 0.495553 | 1.0871 | 0.258993 |
| 1.08577 | 0.857537 | 0.989902 | 4.51445 | 0.582026 |
| 1.08577 | 0 | 1.9798 | 1.50482 | 0.388017 |
| 1.08093 | 0 | 0 | 1.19819 | 0.61806 |
| 1.07895 | 0.0852144 | 0.491838 | 1.12049 | 0.771154 |
| 1.06373 | 0.224035 | 0.969808 | 1.47306 | 0.253427 |
| 1.05582 | 0 | 0.385038 | 1.17033 | 0.301851 |
| 1.05551 | 0.121256 | 0.349931 | 1.06307 | 0.61724 |
| 1.05363 | 0 | 1.28079 | 1.9477 | 0.25102 |
| 1.04745 | 0 | 0.636644 | 1.28951 | 0.415915 |
| 1.03963 | 0.109479 | 0.947835 | 1.92031 | 0.743056 |


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| ---: | ---: | ---: | ---: | ---: |
| 1.03437 | 0.163387 | 0.825153 | 1.07418 | 0.369645 |
| 1.03152 | 0.236999 | 0.512964 | 1.55834 | 0.134046 |
| 1.02788 | 0.12989 | 1.49939 | 1.13854 | 0.477527 |
| 1.02513 | 0.161929 | 1.40192 | 1.42068 | 0.54952 |
| 1.02513 | 0 | 0 | 4.26203 | 1.83173 |
| 1.01635 | 0 | 0.308868 | 1.87726 | 0.726412 |
| 1.01519 | 0.2749 | 1.05777 | 2.41062 | 0.518276 |
| 1.0115 | 0.479325 | 1.61383 | 1.40096 | 1.4459 |
| 1.00589 | 0.0794448 | 0.687806 | 1.39319 | 0.359471 |
| 1.00444 | 0.634642 | 1.0989 | 2.22665 | 0.287162 |
| 1.00267 | 0 | 0.91414 | 2.77903 | 1.07496 |
| 1.00209 | 0.090451 | 1.39217 | 2.37847 | 0.852649 |
| 1.0005 | 0.114936 | 0.49754 | 2.5191 | 0.91011 |

FPKM_rep2_sha FPKM_rep2_shb IPCENPA_rep2_enrich sha_Inp_enrishb_input_elDelta_sha

| 5787.14 | 3463.06 | 3290.235 | 3014.510 | 690.430 | -275.725 |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 167.428 | 159.057 | 133.230 | 100.027 | 91.656 | -33.203 |
| 96.6019 | 114.15 | 95.269 | 54.289 | 71.837 | -40.979 |
| 100.028 | 119.295 | 85.614 | 58.504 | 77.771 | -27.110 |
| 46.7357 | 41.7014 | 42.655 | 25.389 | 20.355 | -17.265 |
| 18.1253 | 15.1583 | 17.235 | 12.117 | 9.150 | -5.118 |
| 16.1698 | 16.6436 | 14.678 | 9.367 | 9.841 | -5.311 |
| 11.0078 | 14.1377 | 12.609 | 5.274 | 8.404 | -7.334 |
| 10.4867 | 9.8225 | 12.129 | 5.018 | 4.354 | -7.111 |
| 12.1542 | 14.366 | 10.260 | 8.287 | 10.498 | -1.974 |
| 16.4865 | 13.3204 | 7.706 | 9.818 | 6.652 | 2.112 |
| 7.46292 | 5.32346 | 9.944 | 4.407 | 2.268 | -5.536 |
| 13.1966 | 12.301 | 8.408 | 8.640 | 7.744 | 0.232 |
| 15.5695 | 15.358 | 9.432 | 12.129 | 11.917 | 2.697 |
| 9.25339 | 6.05636 | 7.914 | 5.253 | 2.056 | -2.662 |
| 7.53506 | 10.7498 | 8.114 | 2.246 | 5.461 | -5.868 |
| 10.3225 | 11.6096 | 6.481 | 6.901 | 8.188 | 0.420 |
| 11.6702 | 9.2951 | 5.547 | 8.907 | 6.532 | 3.360 |
| 5.56406 | 0.84605 | 7.976 | 5.229 | 0.511 | -2.747 |
| 14.4359 | 15.6621 | 5.999 | 8.228 | 9.454 | 2.229 |
| 4.76768 | 3.41764 | 7.381 | 3.639 | 2.289 | -3.742 |
| 7.90158 | 5.62917 | 6.300 | 5.767 | 3.495 | -0.532 |
| 1.83872 | 2.76793 | 6.947 | -0.355 | 0.574 | -7.303 |
| 5.94685 | 5.92983 | 6.119 | 3.672 | 3.655 | -2.446 |
| 8.31002 | 7.28067 | 5.061 | 6.386 | 5.357 | 1.326 |
| 7.88052 | 6.8178 | 5.916 | 6.079 | 5.016 | 0.163 |
| 5.18505 | 6.24427 | 5.325 | 3.260 | 4.319 | -2.065 |
| 4.13043 | 6.04505 | 5.413 | 2.182 | 4.097 | -3.231 |
| 7.82411 | 8.17921 | 5.006 | 6.342 | 6.697 | 1.336 |
| 4.51431 | 6.95461 | 4.917 | 1.837 | 4.277 | -3.081 |
| 0 | 0.787237 | 6.112 | -0.312 | 0.475 | -6.424 |
| 9.87591 | 7.40489 | 5.004 | 6.489 | 4.018 | 1.486 |
| 7.58759 | 8.53369 | 4.598 | 3.078 | 4.024 | -1.520 |
| 0.408662 | 1.36707 | 5.446 | -0.404 | 0.554 | -5.850 |
| 2.81625 | 3.02818 | 5.598 | -0.651 | -0.439 | -6.249 |
| 1.41314 | 1.41818 | 5.339 | 0.664 | 0.669 | -4.676 |
| 6.3908 | 11.1541 | 5.087 | 4.917 | 9.680 | -0.169 |
| 7.14398 | 8.04269 | 4.869 | 5.869 | 6.768 | 1.000 |
| 0.792312 | 7.6201 | 5.144 | -1.571 | 5.256 | -6.716 |
| 4.58089 | 3.0245 | 4.861 | 3.782 | 2.225 | -1.079 |
| 5.19169 | 4.57037 | 4.749 | 3.380 | 2.759 | -1.368 |


| 7.83167 | 3.63872 | 3.387 | 5.092 | 0.899 | 1.704 |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 3.17199 | 4.54759 | 4.070 | 1.169 | 2.545 | -2.901 |
| 4.83622 | 4.35973 | 4.163 | 3.421 | 2.944 | -0.743 |
| 1.66074 | 2.43056 | 4.763 | 0.285 | 1.054 | -4.478 |
| 0 | 6.46751 | 4.931 | -0.961 | 5.506 | -5.893 |
| 4.5113 | 4.71605 | 4.548 | 2.418 | 2.623 | -2.130 |
| 5.95975 | 5.74368 | 3.882 | 3.439 | 3.223 | -0.443 |
| 13.335 | 21.3749 | 2.730 | 4.004 | 12.044 | 1.274 |
| 1.91619 | 6.4101 | 4.163 | 0.963 | 5.457 | -3.199 |
| 0.883165 | 2.21579 | 4.369 | -0.093 | 1.240 | -4.462 |
| 2.51956 | 3.61222 | 3.496 | 1.088 | 2.181 | -2.408 |
| 1.32627 | 1.38647 | 3.140 | 1.106 | 1.167 | -2.033 |
| 3.56692 | 4.41491 | 3.566 | 1.486 | 2.334 | -2.080 |
| 4.9428 | 0 | 4.203 | 3.577 | -1.365 | -0.625 |
| 7.94885 | 5.08352 | 3.553 | 5.159 | 2.294 | 1.606 |
| 7.86983 | 4.73052 | 3.241 | 7.381 | 4.241 | 4.139 |
| 2.94388 | 1.231 | 3.923 | 2.554 | 0.841 | -1.370 |
| 2.40718 | 3.85852 | 3.741 | 1.343 | 2.795 | -2.397 |
| 3.16311 | 2.64533 | 3.495 | 1.447 | 0.930 | -2.048 |
| 4.27842 | 2.99257 | 3.558 | 1.958 | 0.672 | -1.600 |
| 3.29971 | 3.90147 | 3.558 | 1.867 | 2.468 | -1.691 |
| 2.60095 | 2.57068 | 2.839 | 1.660 | 1.630 | -1.179 |
| 1.21352 | 1.52231 | 3.584 | 1.012 | 1.321 | -2.572 |
| 4.18013 | 2.91323 | 3.673 | 2.910 | 1.643 | -0.763 |
| 2.08552 | 5.52311 | 3.461 | 1.625 | 5.062 | -1.837 |
| 2.90629 | 3.47222 | 3.364 | 2.356 | 2.922 | -1.009 |
| 0.902261 | 1.50914 | 3.369 | 0.155 | 0.761 | -3.215 |
| 6.00379 | 4.54283 | 2.372 | 3.540 | 2.079 | 1.168 |
| 4.31039 | 6.37774 | 3.302 | 2.552 | 4.619 | -0.750 |
| 3.36873 | 1.32579 | 3.444 | 3.237 | 1.194 | -0.206 |
| 2.36735 | 3.51971 | 2.426 | 2.193 | 3.345 | -0.233 |
| 0.327243 | 1.91573 | 3.451 | -0.107 | 1.482 | -3.557 |
| 1.19888 | 1.00263 | 3.438 | 1.000 | 0.804 | -2.438 |
| 2.05853 | 1.53028 | 3.204 | 0.997 | 0.469 | -2.207 |
| 2.7666 | 1.24586 | 2.929 | 1.074 | -0.447 | -1.856 |
| 1.72606 | 1.44351 | 3.522 | 1.497 | 1.215 | -2.025 |
| 1.76573 | 1.05478 | 2.770 | 1.431 | 0.720 | -1.339 |
| 3.11103 | 3.64249 | 2.977 | 1.461 | 1.993 | -1.515 |
| 2.75758 | 1.92182 | 3.141 | 2.453 | 1.617 | -0.688 |
| 2.69177 | 2.8651 | 3.261 | 1.556 | 1.730 | -1.705 |
| 3.64283 | 3.45273 | 3.023 | 2.435 | 2.245 | -0.588 |
| 5.15103 | 6.46177 | 2.680 | 3.832 | 5.142 | 1.152 |


| 0.988177 | 1.37737 | 3.168 | 0.551 | 0.941 | -2.616 |
| ---: | ---: | ---: | ---: | ---: | ---: |
| 4.03355 | 3.81714 | 2.788 | 2.978 | 2.762 | 0.190 |
| 0.654486 | 0.273676 | 3.147 | 0.221 | -0.160 | -2.926 |
| 2.12748 | 1.69835 | 3.149 | 0.974 | 0.544 | -2.175 |
| 0.630222 | 1.05412 | 3.189 | 0.212 | 0.636 | -2.977 |
| 1.61511 | 1.89102 | 2.917 | 0.330 | 0.606 | -2.587 |
| 0.320951 | 1.07365 | 3.275 | 0.321 | 1.074 | -2.954 |
| 1.63154 | 2.33909 | 2.970 | 1.168 | 1.876 | -1.802 |
| 2.38445 | 2.34094 | 2.626 | 1.216 | 1.173 | -1.410 |
| 3.87026 | 2.28475 | 2.367 | 3.267 | 1.681 | 0.900 |
| 1.57254 | 1.31513 | 2.754 | -0.252 | -0.509 | -3.006 |
| 4.98222 | 2.43056 | 2.837 | 4.707 | 2.155 | 1.870 |
| 4.40973 | 4.97865 | 2.809 | 3.825 | 4.394 | 1.016 |
| 2.76705 | 2.89264 | 2.642 | 1.277 | 1.402 | -1.366 |
| 3.07105 | 2.56834 | 2.577 | 0.399 | -0.104 | -2.178 |
| 3.89125 | 3.54143 | 2.355 | 1.919 | 1.569 | -0.436 |
| 0 | 0.492398 | 3.004 | -0.195 | 0.297 | -3.199 |
| 5.08782 | 1.54727 | 3.003 | 4.475 | 0.934 | 1.471 |
| 0.910649 | 0.951978 | 2.423 | 0.156 | 0.197 | -2.267 |
| 4.75387 | 1.98785 | 2.940 | 4.491 | 1.725 | 1.552 |
| 2.92191 | 3.05452 | 2.793 | 1.469 | 1.602 | -1.324 |
| 4.3007 | 4.34085 | 2.628 | 2.924 | 2.964 | 0.296 |
| 4.3534 | 1.56034 | 1.973 | 3.735 | 0.942 | 1.762 |
| 4.25945 | 3.88605 | 2.646 | 2.206 | 1.832 | -0.441 |
| 0.772598 | 2.15377 | 2.565 | -0.081 | 1.300 | -2.646 |
| 2.25686 | 3.77486 | 2.554 | 0.829 | 2.347 | -1.725 |
| 1.81251 | 0.816209 | 2.355 | 1.443 | 0.446 | -0.912 |
| 0.655553 | 0.730992 | 2.709 | 0.511 | 0.586 | -2.199 |
| 0.47063 | 0.787183 | 2.837 | 0.471 | 0.787 | -2.367 |
| 3.03494 | 3.3842 | 1.926 | -0.989 | -0.640 | -2.915 |
| 2.67257 | 3.77172 | 2.593 | 2.230 | 3.329 | -0.363 |
| 0.897966 | 3.12907 | 2.601 | -0.094 | 2.137 | -2.695 |
| 2.13745 | 0.893785 | 2.400 | 1.571 | 0.327 | -0.829 |
| 1.63045 | 0.90904 | 2.773 | 0.910 | 0.188 | -1.863 |
| 3.40778 | 5.05091 | 2.042 | 2.178 | 3.821 | 0.135 |
| 2.23634 | 2.0947 | 2.214 | 1.169 | 1.027 | -1.045 |
| 6.21762 | 6.02087 | 1.88021 | 3.614 | 3.418 | 2.033 |
| 0.864704 | 1.92429 | 0.635 | 1.651 | -1.585 |  |
| 1.6734 | 4.58193 | 0.287 | 0.538 | -2.307 |  |
| 0.104663 | 3.09628 | 2.645 | -1.222 |  |  |
| 2.64452 |  | 0.534 | -2.279 |  |  |
|  |  | 2.921 | 0.236 |  |  |
|  |  |  |  |  |  |


| 4.35007 | 4.24433 | 2.265 | 2.428 | 2.322 | 0.163 |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 3.55985 | 1.11642 | 2.292 | 2.675 | 0.231 | 0.383 |
| 1.2838 | 2.68414 | 2.679 | 1.284 | 2.684 | -1.395 |
| 0.616974 | 2.23592 | 2.309 | -0.337 | 1.282 | -2.646 |
| 2.72727 | 1.9007 | 2.226 | 2.426 | 1.599 | 0.200 |
| 3.85884 | 2.88747 | 2.399 | 2.512 | 1.541 | 0.113 |
| 4.13183 | 1.94371 | 2.256 | 2.762 | 0.574 | 0.506 |
| 2.49331 | 2.71467 | 2.370 | 1.807 | 2.029 | -0.563 |
| 0.649751 | 3.44148 | 2.612 | 0.506 | 3.298 | -2.105 |
| 0.932872 | 1.56034 | 2.596 | 0.521 | 1.148 | -2.075 |
| 1.39184 | 1.16401 | 2.310 | 0.930 | 0.703 | -1.380 |
| 1.39035 | 3.19759 | 2.172 | -0.223 | 1.585 | -2.394 |
| 2.01798 | 3.3753 | 2.278 | 1.182 | 2.539 | -1.096 |
| 2.76736 | 1.58351 | 2.396 | 1.995 | 0.811 | -0.401 |
| 5.29734 | 4.253 | 2.058 | 4.735 | 3.691 | 2.677 |
| 4.27337 | 1.78693 | 2.369 | 3.464 | 0.978 | 1.095 |
| 2.32078 | 0.529333 | 2.420 | 2.041 | 0.250 | -0.379 |
| 4.39739 | 1.98023 | 2.312 | 3.949 | 1.532 | 1.637 |
| 5.11333 | 2.64725 | 1.485 | 4.306 | 1.840 | 2.821 |
| 4.33903 | 3.07049 | 2.281 | 2.348 | 1.079 | 0.067 |
| 3.5603 | 2.06135 | 1.921 | 2.592 | 1.093 | 0.671 |
| 0.658493 | 0.734271 | 1.929 | 0.513 | 0.589 | -1.416 |
| 2.47015 | 3.61516 | 1.801 | 0.935 | 2.080 | -0.866 |
| 2.61355 | 4.57017 | 1.867 | 1.196 | 3.153 | -0.671 |
| 0.174172 | 0.436985 | 2.321 | -0.403 | -0.140 | -2.724 |
| 4.47748 | 3.74455 | 1.548 | 2.993 | 2.260 | 1.445 |
| 1.25893 | 0.912472 | 2.315 | 1.203 | 0.857 | -1.112 |
| 2.31737 | 0.912016 | 2.163 | 1.956 | 0.551 | -0.207 |
| 0.994832 | 0.665589 | 2.166 | -0.324 | -0.653 | -2.490 |
| 3.87627 | 4.32234 | 1.829 | 2.163 | 2.609 | 0.334 |
| 0.789444 | 1.98065 | 2.148 | -0.519 | 0.672 | -2.667 |
| 1.7593 | 0.936292 | 2.280 | 1.229 | 0.406 | -1.051 |
| 1.4185 | 2.96575 | 2.285 | 0.854 | 2.402 | -1.431 |
| 6.05917 | 1.60021 | 1.993 | 5.636 | 1.177 | 3.644 |
| 3.20027 | 2.67641 | 2.097 | 2.363 | 1.839 | 0.266 |
| 1.87745 | 4.97207 | 1.955 | 0.425 | 3.520 | -1.530 |
| 0.616974 | 1.54794 | 1.927 | 0.344 | 1.275 | -1.583 |
| 2.64079 | 2.06128 | 2.183 | 2.524 | 1.945 | 0.341 |
| 3.35259 | 1.68228 | 1.756 | 2.760 | 1.090 | 1.003 |
| 1.39035 | 4.94173 | 1.442 | 0.238 | 3.790 | -1.204 |
| 5.74857 | 6.00947 | 1.379 | 4.161 | 4.422 | 2.781 |
| 1.07342 | 2.69312 | 1.561 | 0.362 | 1.982 | -1.199 |


| 1.47194 | 2.95439 | 2.012 | 1.082 | 2.564 | -0.930 |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 0.47063 | 2.36155 | 1.907 | -0.465 | 1.426 | -2.372 |
| 3.32828 | 4.4208 | 1.950 | 1.901 | 2.993 | -0.049 |
| 3.38335 | 4.57076 | 1.410 | 1.140 | 2.328 | -0.270 |
| 1.48326 | 0.708834 | 2.038 | 0.781 | 0.006 | -1.257 |
| 0.932308 | 1.16955 | 2.025 | 0.314 | 0.551 | -1.711 |
| 1.15987 | 1.35801 | 2.016 | 0.545 | 0.743 | -1.471 |
| 1.75529 | 2.49866 | 1.863 | 1.211 | 1.954 | -0.653 |
| 0.630222 | 1.05412 | 2.020 | 0.352 | 0.776 | -1.669 |
| 1.1544 | 1.93088 | 1.465 | 0.848 | 1.625 | -0.617 |
| 3.95271 | 1.10189 | 1.946 | 3.298 | 0.447 | 1.352 |
| 0.862666 | 2.64533 | 2.134 | 0.291 | 2.073 | -1.843 |
| 0.344609 | 0.960664 | 2.064 | -0.188 | 0.428 | -2.252 |
| 2.91599 | 1.56771 | 2.003 | 2.088 | 0.739 | 0.084 |
| 4.5814 | 4.10514 | 1.741 | 2.846 | 2.370 | 1.105 |
| 3.3524 | 4.55084 | 1.634 | 2.547 | 3.746 | 0.913 |
| 2.54679 | 2.95196 | 1.852 | 1.362 | 1.767 | -0.490 |
| 1.6256 | 2.1752 | 1.539 | 0.979 | 1.529 | -0.560 |
| 2.45757 | 1.71273 | 1.849 | 2.322 | 1.577 | 0.472 |
| 3.2825 | 2.99474 | 1.639 | 2.788 | 2.500 | 1.149 |
| 2.68207 | 4.673 | 1.811 | 1.941 | 3.932 | 0.130 |
| 6.25775 | 4.11196 | 2.073 | 5.961 | 3.816 | 3.888 |
| 2.23233 | 5.06733 | 1.697 | 1.810 | 4.645 | 0.113 |
| 2.85359 | 3.6448 | 1.492 | 1.340 | 2.131 | -0.151 |
| 1.33494 | 0.930353 | 2.064 | 0.892 | 0.488 | -1.171 |
| 3.95472 | 3.51408 | 1.629 | 2.644 | 2.203 | 1.015 |
| 5.18582 | 4.02716 | 1.844 | 4.204 | 3.045 | 2.359 |
| 0.604272 | 1.85298 | 2.055 | 0.337 | 1.586 | -1.718 |
| 1.80538 | 1.50986 | 1.694 | 1.539 | 1.244 | -0.155 |
| 0.735488 | 3.38302 | 2.047 | -0.240 | 2.408 | -2.286 |
| 1.39828 | 2.07892 | 1.653 | 0.780 | 1.461 | -0.873 |
| 2.15963 | 3.91324 | 1.581 | 0.728 | 2.482 | -0.853 |
| 2.14151 | 2.68644 | 1.986 | 2.071 | 2.615 | 0.084 |
| 2.74716 | 4.0844 | 1.982 | 1.938 | 3.275 | -0.044 |
| 3.35764 | 1.78693 | 1.445 | 2.144 | 0.573 | 0.698 |
| 0.818412 | 1.91644 | 1.878 | 0.601 | 1.699 | -1.276 |
| 1.59527 | 4.44714 | 1.973 | 1.066 | 3.918 | -0.906 |
| 2.92467 | 1.11178 | 1.505 | 2.220 | 0.407 | 0.714 |
| 1.31431 | 1.26827 | 1.910 | 0.912 | 0.866 | -0.998 |
| 0.560892 | 1.05543 | 1.951 | 0.189 | 0.684 | -1.762 |
| 3.29692 | 1.50395 | 1.770 | 3.297 | 1.504 | 1.527 |
| 2.43078 | 1.86931 | 1.682 | 1.912 | 1.351 | 0.230 |


| 0.951981 | 1.43307 | 1.664 | 0.573 | 1.054 | -1.090 |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 0.409594 | 0.856367 | 1.900 | 0.138 | 0.585 | -1.762 |
| 2.04329 | 4.27205 | 1.496 | 1.818 | 4.046 | 0.321 |
| 7.14753 | 0.853934 | 1.595 | 6.809 | 0.515 | 5.214 |
| 2.70609 | 3.39469 | 1.684 | 2.482 | 3.170 | 0.798 |
| 2.37989 | 2.18609 | 1.562 | 1.371 | 1.177 | -0.190 |
| 2.81994 | 1.51607 | 1.514 | 1.752 | 0.448 | 0.238 |
| 2.26067 | 1.55698 | 1.383 | 1.732 | 1.028 | 0.349 |
| 1.53384 | 1.92414 | 1.580 | 0.263 | 0.653 | -1.317 |
| 1.29556 | 1.08349 | 1.732 | 0.833 | 0.621 | -0.899 |
| 3.16925 | 2.31916 | 1.837 | 2.119 | 1.269 | 0.282 |
| 2.29377 | 3.37986 | 1.632 | 1.063 | 2.149 | -0.569 |
| 2.16225 | 1.8083 | 1.823 | 0.859 | 0.505 | -0.964 |
| 0.838298 | 5.84229 | 1.487 | -1.199 | 3.805 | -2.686 |
| 1.56064 | 2.28405 | 1.352 | -0.250 | 0.474 | -1.602 |
| 1.55959 | 1.38582 | 1.408 | 0.978 | 0.804 | -0.430 |
| 2.40661 | 2.97108 | 1.538 | 1.571 | 2.135 | 0.033 |
| 1.34233 | 1.23487 | 1.609 | 0.541 | 0.434 | -1.067 |
| 2.28496 | 1.91093 | 1.341 | 1.780 | 1.406 | 0.439 |
| 2.39524 | 5.60883 | 1.216 | 1.443 | 4.656 | 0.227 |
| 0.273247 | 2.51371 | 1.614 | -0.089 | 2.151 | -1.703 |
| 8.83383 | 0.599011 | -0.887 | 6.935 | -1.300 | 7.821 |
| 1.89882 | 2.82311 | 1.638 | 1.479 | 2.404 | -0.158 |
| 2.70253 | 3.39022 | 1.280 | 1.807 | 2.494 | 0.527 |
| 1.773 | 1.87819 | 1.477 | 1.146 | 1.251 | -0.331 |
| 2.10074 | 2.98667 | 1.507 | 0.430 | 1.315 | -1.078 |
| 5.63801 | 0.628682 | 1.523 | 5.140 | 0.130 | 3.617 |
| 1.06966 | 1.90095 | 1.501 | 0.361 | 1.192 | -1.141 |
| 1.24143 | 1.81688 | 1.545 | 0.967 | 1.543 | -0.578 |
| 0.547357 | 1.92259 | 1.470 | -0.033 | 1.342 | -1.503 |
| 0 | 0.721604 | 1.643 | -0.409 | 0.313 | -2.051 |
| 1.83144 | 2.80803 | 1.341 | 1.629 | 2.606 | 0.288 |
| 1.59693 | 2.28947 | 1.425 | 0.916 | 1.609 | -0.509 |
| 1.67138 | 2.41436 | 1.483 | 1.235 | 1.978 | -0.249 |
| 1.26201 | 2.22812 | 1.198 | -0.039 | 0.927 | -1.237 |
| 2.40662 | 1.81968 | 1.353 | 1.379 | 0.792 | 0.026 |
| 0.799116 | 2.172 | 1.668 | 0.534 | 1.907 | -1.133 |
| 1.34719 | 0.751108 | 1.534 | 0.305 | -0.291 | -1.229 |
| 0.975565 | 1.49577 | 1.468 | 0.544 | 1.065 | -0.924 |
| 2.8035 | 0.852577 | 1.655 | 2.297 | 0.346 | 0.642 |
| 0.969123 | 1.08065 | 1.459 | 0.220 | 0.331 | -1.239 |
| 1.4196 | 3.56168 | 1.646 | 0.714 | 2.856 | -0.932 |


| 1.77451 | 2.96807 | 1.438 | 1.775 | 2.968 | 0.337 |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 1.22684 | 0.456008 | 1.324 | 0.414 | -0.357 | -0.911 |
| 2.15359 | 0.818667 | 1.290 | 1.505 | 0.170 | 0.215 |
| 1.57545 | 2.1701 | 1.416 | 0.961 | 1.556 | -0.455 |
| 2.1725 | 1.29777 | 1.510 | 1.692 | 0.818 | 0.182 |
| 1.75828 | 1.71554 | 1.373 | 1.273 | 1.230 | -0.101 |
| 1.29497 | 1.62449 | 1.522 | 0.804 | 1.134 | -0.717 |
| 1.5927 | 1.78986 | 1.412 | 0.933 | 1.130 | -0.479 |
| 1.38077 | 2.96217 | 1.369 | 0.784 | 2.365 | -0.585 |
| 3.22947 | 2.70083 | 1.176 | 2.571 | 2.042 | 1.395 |
| 0.712119 | 0.595551 | 1.366 | 0.240 | 0.123 | -1.126 |
| 2.41648 | 3.75314 | 1.399 | 1.272 | 2.609 | -0.126 |
| 2.70525 | 1.02837 | 1.453 | 1.890 | 0.213 | 0.437 |
| 0.489412 | 2.25115 | 1.302 | -0.159 | 1.602 | -1.461 |
| 0.978824 | 2.66045 | 1.589 | 0.330 | 2.012 | -1.259 |
| 1.21252 | 1.90878 | 1.421 | 0.598 | 1.294 | -0.823 |
| 0.74789 | 1.78705 | 1.586 | 0.323 | 1.362 | -1.263 |
| 1.23872 | 1.29494 | 1.262 | 0.931 | 0.987 | -0.331 |
| 2.64564 | 0.790204 | 1.578 | 1.894 | 0.039 | 0.316 |
| 1.41314 | 3.07273 | 1.407 | 1.038 | 2.698 | -0.369 |
| 1.35479 | 2.26604 | 1.372 | 0.681 | 1.592 | -0.691 |
| 0.84619 | 1.65124 | 1.487 | 0.472 | 1.277 | -1.015 |
| 4.82198 | 7.46043 | 1.424 | 2.744 | 5.383 | 1.320 |
| 1.18135 | 1.41139 | 1.466 | 0.398 | 0.628 | -1.068 |
| 0.843793 | 0.352835 | 0.329 | 0.844 | 0.353 | 0.515 |
| 0.840296 | 1.93255 | 1.313 | 0.423 | 1.515 | -0.890 |
| 0.955009 | 1.19802 | 0.851 | 0.322 | 0.565 | -0.529 |
| 3.58128 | 2.99506 | 1.410 | 1.682 | 1.096 | 0.272 |
| 2.14877 | 3.19473 | 1.410 | 0.724 | 1.770 | -0.686 |
| 6.00789 | 1.95395 | 1.548 | 4.902 | 0.848 | 3.354 |
| 1.66628 | 1.91609 | 1.057 | 0.976 | 1.226 | -0.081 |
| 1.56169 | 2.00262 | 1.423 | 1.217 | 1.658 | -0.206 |
| 1.15808 | 1.21064 | 1.502 | 0.966 | 1.019 | -0.536 |
| 0.994705 | 3.05023 | 1.538 | 0.555 | 2.611 | -0.983 |
| 2.75528 | 1.75124 | 1.081 | 2.171 | 1.167 | 1.090 |
| 1.55483 | 1.83574 | 1.259 | 0.949 | 1.229 | -0.310 |
| 2.87921 | 3.09588 | 1.285 | 2.061 | 2.278 | 0.776 |
| 0.596818 | 0.499124 | 1.435 | 0.399 | 0.301 | -1.036 |
| 1.63933 | 2.15441 | 1.109 | 1.329 | 1.844 | 0.220 |
| 0.702413 | 0.685339 | 1.383 | 0.470 | 0.453 | -0.913 |
| 1.42168 | 2.20807 | 1.269 | 1.018 | 1.804 | -0.251 |
| 2.12456 | 1.41098 | 1.177 | 1.917 | 1.204 | 0.740 |


| 1.39184 | 2.71602 | 1.234 | 0.777 | 2.101 | -0.458 |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 0.499345 | 0.208803 | 1.432 | 0.086 | -0.205 | -1.347 |
| 1.81695 | 1.35672 | 1.353 | 1.043 | 0.582 | -0.310 |
| 4.0547 | 4.06917 | 1.504 | 3.517 | 3.532 | 2.013 |
| 3.03385 | 1.86064 | 1.264 | 2.498 | 1.324 | 1.234 |
| 1.91052 | 1.22907 | 1.499 | 0.839 | 0.157 | -0.661 |
| 3.46321 | 2.31705 | 1.364 | 3.004 | 1.858 | 1.640 |
| 2.50679 | 3.1866 | 1.077 | 0.911 | 1.591 | -0.165 |
| 0.933232 | 1.1707 | 1.367 | 0.624 | 0.861 | -0.743 |
| 1.158 | 1.61408 | 1.420 | 0.806 | 1.262 | -0.614 |
| 1.07882 | 1.11451 | 1.137 | 0.153 | 0.189 | -0.984 |
| 1.05687 | 1.76774 | 1.470 | 0.286 | 0.997 | -1.184 |
| 2.17097 | 2.80593 | 1.349 | 1.909 | 2.544 | 0.560 |
| 1.15756 | 0.616048 | 1.402 | 1.018 | 0.477 | -0.384 |
| 0.979616 | 1.36544 | 1.336 | 0.366 | 0.752 | -0.970 |
| 0.899939 | 2.35196 | 1.197 | 0.751 | 2.203 | -0.446 |
| 2.62192 | 0.438546 | 1.357 | 2.158 | -0.025 | 0.802 |
| 0.845795 | 1.31364 | 1.457 | 0.766 | 1.234 | -0.691 |
| 1.34104 | 3.17764 | 1.189 | 0.748 | 2.585 | -0.441 |
| 2.08241 | 1.52384 | 1.449 | 1.824 | 1.265 | 0.375 |
| 1.04103 | 2.39421 | 1.296 | 0.696 | 2.049 | -0.600 |
| 1.29805 | 1.41124 | 1.369 | 0.868 | 0.981 | -0.501 |
| 1.33494 | 2.79106 | 1.184 | 0.597 | 2.054 | -0.586 |
| 1.81222 | 3.24765 | 0.379 | 1.126 | 2.561 | 0.747 |
| 0.664452 | 2.40797 | 1.178 | 0.077 | 1.821 | -1.101 |
| 1.96877 | 3.17538 | 1.270 | 0.850 | 2.057 | -0.420 |
| 1.54515 | 1.55066 | 1.071 | 0.726 | 0.731 | -0.345 |
| 2.47015 | 3.22782 | 1.341 | 1.140 | 1.897 | -0.202 |
| 1.43275 | 0.368683 | 1.237 | 1.214 | 0.149 | -0.024 |
| 3.33049 | 3.85659 | 1.125 | 2.142 | 2.668 | 1.016 |
| 3.68548 | 0.5137 | 1.424 | 2.260 | -0.912 | 0.836 |
| 0.510538 | 2.13484 | 0.822 | -0.166 | 1.458 | -0.989 |
| 1.26481 | 1.22478 | 1.342 | 0.779 | 0.739 | -0.563 |
| 1.33833 | 2.87809 | 1.307 | 1.212 | 2.751 | -0.095 |
| 1.30528 | 2.36517 | 1.412 | 1.017 | 2.077 | -0.396 |
| 4.24731 | 4.31321 | 1.229 | 3.041 | 3.106 | 1.811 |
| 1.81257 | 0.63161 | 1.224 | 1.412 | 0.231 | 0.188 |
| 1.60106 | 1.50635 | 0.923 | 1.336 | 1.241 | 0.413 |
| 3.32935 | 2.08827 | 0.902 | 2.778 | 1.536 | 1.876 |
| 1.24842 | 2.08812 | 1.390 | 1.083 | 1.923 | -0.307 |
| 1.12086 | 2.03099 | 1.277 | 0.625 | 1.536 | -0.651 |
| 1.06408 | 1.06788 | 1.132 | 0.923 | 0.927 | -0.209 |


| 0.595845 | 3.73733 | 1.032 | -0.589 | 2.552 | -1.622 |
| ---: | ---: | ---: | ---: | ---: | ---: |
| 1.11125 | 3.4076 | 1.374 | 0.620 | 2.916 | -0.754 |
| 1.55985 | 1.64781 | 1.130 | 1.179 | 1.267 | 0.049 |
| 0.943037 | 1.48971 | 1.238 | -0.168 | 0.378 | -1.406 |
| 1.05704 | 1.0103 | 1.265 | 0.490 | 0.443 | -0.776 |
| 0.971421 | 1.72637 | 1.209 | 0.488 | 1.243 | -0.721 |
| 0.581867 | 2.4331 | 1.179 | 0.196 | 2.047 | -0.983 |
| 3.06889 | 1.08065 | 1.348 | 2.641 | 0.652 | 1.292 |
| 3.98756 | 3.638 | 1.132 | 3.507 | 3.157 | 2.374 |
| 4.7984 | 2.00647 | 1.054 | 4.480 | 1.688 | 3.426 |
| 0.913483 | 1.63704 | 1.026 | 0.394 | 1.118 | -0.631 |
| 1.63838 | 1.88401 | 0.490 | 1.231 | 1.477 | 0.742 |
| 1.54008 | 1.68428 | 1.076 | 0.637 | 0.781 | -0.439 |
| 0.848636 | 2.01088 | 1.146 | 0.567 | 1.730 | -0.579 |
| 1.97444 | 2.24097 | 0.978 | 1.413 | 1.680 | 0.436 |
| 1.8763 | 1.04611 | 1.214 | 1.669 | 0.839 | 0.455 |
| 1.6766 | 2.8043 | 1.132 | 1.121 | 2.249 | -0.011 |
| 1.04133 | 1.74174 | 0.881 | -0.339 | 0.361 | -1.220 |
| 0.766918 | 1.3469 | 1.191 | 0.360 | 0.940 | -0.830 |
| 1.44514 | 1.38124 | 0.954 | 1.080 | 1.016 | 0.126 |
| 2.75041 | 1.72514 | 1.074 | 1.231 | 0.206 | 0.157 |
| 1.48633 | 3.05976 | 1.139 | 0.349 | 1.923 | -0.789 |
| 0.747111 | 1.14549 | 1.197 | 0.334 | 0.733 | -0.863 |
| 2.27662 | 2.09435 | 1.134 | 1.673 | 1.491 | 0.539 |
| 0.227662 | 2.47514 | 1.134 | -0.225 | 2.022 | -1.359 |
| 2.5529 | 2.70434 | 1.226 | 0.796 | 2.128 | -0.430 |
| 1.25202 | 0.698049 | 0.930 | 1.932 | 0.485 | 0.201 |


| 1.00375 | 1.69714 | 1.061 | 0.555 | 1.249 | -0.506 |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 0 | 2.71696 | 0.951 | -0.431 | 2.286 | -1.382 |
| 0.830912 | 1.54422 | 1.145 | 0.341 | 1.055 | -0.803 |
| 4.17236 | 0.805241 | 0.626 | 3.321 | -0.046 | 2.695 |
| 0.512382 | 2.3568 | 1.188 | -0.337 | 1.508 | -1.525 |
| 1.17015 | 1.06757 | 0.997 | 0.747 | 0.644 | -0.250 |
| 2.87013 | 3.46712 | 1.183 | 2.659 | 3.256 | 1.476 |
| 1.27432 | 3.19716 | 1.033 | 0.936 | 2.859 | -0.096 |
| 1.38054 | 1.01601 | 1.081 | 0.868 | 0.503 | -0.213 |
| 0.930368 | 0.869613 | 1.103 | 0.422 | 0.362 | -0.681 |
| 0.993125 | 0.775188 | 1.012 | 0.379 | 0.161 | -0.633 |
| 0.250959 | 2.72843 | 1.164 | 0.251 | 2.728 | -0.913 |
| 2.90363 | 2.60178 | 0.668 | 2.354 | 2.052 | 1.686 |
| 0.619579 | 2.59079 | 0.665 | 0.346 | 2.317 | -0.319 |
| 2.22453 | 2.68724 | 1.001 | 1.733 | 2.196 | 0.732 |
| 0.841628 | 1.22002 | 0.948 | -0.200 | 0.179 | -1.148 |
| 3.08487 | 3.09588 | 0.903 | 2.540 | 2.551 | 1.636 |
| 1.79164 | 0.936475 | 1.077 | 1.049 | 0.194 | -0.028 |
| 3.19712 | 2.67377 | 1.141 | 2.382 | 1.859 | 1.241 |
| 2.11306 | 2.04619 | 1.004 | 1.892 | 1.825 | 0.888 |
| 1.83144 | 2.80803 | 1.132 | 0.820 | 1.796 | -0.313 |
| 0.729089 | 1.15174 | 1.032 | 0.192 | 0.615 | -0.840 |
| 1.21145 | 2.22892 | 0.840 | 1.211 | 2.229 | 0.372 |
| 1.05733 | 1.38954 | 0.855 | 0.457 | 0.789 | -0.399 |
| 1.54782 | 1.8919 | 0.965 | 0.759 | 1.103 | -0.206 |
| 0.71092 | 1.09 | 1.030 | 0.083 | 0.462 | -0.947 |
| 1.65881 | 1.09 | 0.960 | 1.188 | 0.619 | 0.227 |
| 3.55374 | 1.73368 | 1.099 | 2.179 | 0.359 | 1.081 |
| 2.8374 | 1.38421 | 0.819 | 2.524 | 1.071 | 1.704 |
| 0.983805 | 0.548509 | 1.018 | 0.723 | 0.288 | -0.295 |
| 1.37598 | 2.13709 | 0.979 | 0.594 | 1.355 | -0.385 |
| 1.66037 | 0.163363 | 1.087 | 1.401 | -0.096 | 0.314 |
| 4.38976 | 2.93696 | 0.228 | 3.808 | 2.355 | 3.580 |
| 2.34121 | 2.44746 | 1.086 | 1.953 | 2.059 | 0.867 |
| 0.932308 | 1.55939 | 1.081 | 0.314 | 0.941 | -0.767 |
| 0.508918 | 1.33764 | 0.994 | -0.262 | 0.566 | -1.256 |
| 1.24241 | 1.03904 | 0.840 | 0.989 | 0.786 | 0.149 |
| 2.27662 | 0.951978 | 1.056 | 1.975 | 0.650 | 0.919 |
| 0.413809 | 0.951698 | 0.934 | -0.203 | 0.334 | -1.138 |
| 3.40784 | 3.48334 | 1.054 | 3.157 | 3.232 | 2.103 |
| 2.63501 | 2.62343 | 1.047 | 2.219 | 2.208 | 1.172 |
| 2.42852 | 0.937382 | 0.930 | 1.685 | 0.194 | 0.755 |


| 1.46367 | 1.39895 | 0.871 | 1.094 | 1.029 | 0.223 |
| ---: | ---: | ---: | ---: | ---: | ---: |
| 1.21321 | 0.930063 | 0.795 | 1.079 | 0.796 | 0.285 |
| 1.27442 | 1.06581 | 0.898 | 0.797 | 0.588 | -0.101 |
| 3.03937 | 1.61754 | 0.863 | 2.490 | 1.068 | 1.627 |
| 0.828919 | 5.31478 | 1.025 | -1.003 | 3.483 | -2.028 |
| 0.730501 | 1.83277 | 1.016 | 0.004 | 1.106 | -1.012 |
| 0.78179 | 1.83069 | 0.740 | 0.264 | 1.312 | -0.477 |
| 0.545263 | 2.05204 | 0.532 | -0.901 | 0.606 | -1.433 |
| 1.49116 | 1.70055 | 0.926 | 1.132 | 1.341 | 0.205 |
| 1.2995 | 4.34713 | 0.370 | 1.012 | 4.060 | 0.643 |
| 0 | 2.48616 | 1.003 | -1.075 | 1.411 | -2.078 |
| 1.18328 | 2.23732 | 0.912 | 0.331 | 1.385 | -0.581 |
| 2.94182 | 0.73808 | 0.886 | 2.032 | -0.172 | 1.146 |


| Delta_shb | Delta_sha_p Delta_shb_perc |  |
| ---: | ---: | ---: |
| -2599.805 | $-8.38 \%$ | $-79.02 \%$ |
| -41.574 | $-24.92 \%$ | $-31.20 \%$ |
| -23.431 | $-43.01 \%$ | $-24.59 \%$ |
| -7.843 | $-31.67 \%$ | $-9.16 \%$ |
| -22.300 | $-40.48 \%$ | $-52.28 \%$ |
| -8.085 | $-29.69 \%$ | $-46.91 \%$ |
| -4.837 | $-36.18 \%$ | $-32.96 \%$ |
| -4.205 | $-58.17 \%$ | $-33.35 \%$ |
| -7.775 | $-58.63 \%$ | $-64.11 \%$ |
| 0.238 | $-19.23 \%$ | $2.32 \%$ |
| -1.054 | $27.40 \%$ | $-13.68 \%$ |
| -7.676 | $-55.68 \%$ | $-77.19 \%$ |
| -0.663 | $2.76 \%$ | $-7.89 \%$ |
| 2.485 | $28.59 \%$ | $26.35 \%$ |
| -5.859 | $-33.63 \%$ | $-74.03 \%$ |
| -2.653 | $-72.32 \%$ | $-32.70 \%$ |
| 1.707 | $6.48 \%$ | $26.34 \%$ |
| 0.985 | $60.58 \%$ | $17.76 \%$ |
| -7.465 | $-34.44 \%$ | $-93.60 \%$ |
| 3.455 | $37.16 \%$ | $57.60 \%$ |
| -5.092 | $-50.70 \%$ | $-68.99 \%$ |
| -2.805 | $-8.45 \%$ | $-44.52 \%$ |
| -6.374 | $-105.12 \%$ | $-91.74 \%$ |
| -2.463 | $-39.98 \%$ | $-40.26 \%$ |
| 0.296 | $26.19 \%$ | $5.85 \%$ |
| -0.900 | $2.75 \%$ | $-15.21 \%$ |
| -1.006 | $-38.78 \%$ | $-18.89 \%$ |
| -1.316 | $-59.69 \%$ | $-24.31 \%$ |
| 1.692 | $26.70 \%$ | $33.79 \%$ |
| -0.640 | $-62.65 \%$ | $-13.02 \%$ |
| -5.637 | $-105.11 \%$ | $-92.22 \%$ |
| -0.985 | $29.70 \%$ | $-19.69 \%$ |
| -0.574 | $-33.06 \%$ | $-12.48 \%$ |
| -4.892 | $-107.42 \%$ | $-89.82 \%$ |
| -6.037 | $-111.63 \%$ | $-107.84 \%$ |
| -4.671 | $-87.57 \%$ | $-87.48 \%$ |
| 4.594 | $-3.33 \%$ | $90.31 \%$ |
| 1.899 | $20.54 \%$ | $39.00 \%$ |
| 0.112 | $-130.55 \%$ | $2.18 \%$ |
| -1.990 | $-22.20 \%$ | $-54.22 \%$ |
|  | $-28.82 \%$ | $-41.90 \%$ |


| -2.489 | $50.32 \%$ | $-73.47 \%$ |
| ---: | ---: | ---: |
| -1.525 | $-71.27 \%$ | $-37.47 \%$ |
| -1.219 | $-17.84 \%$ | $-29.29 \%$ |
| -3.709 | $-94.03 \%$ | $-77.86 \%$ |
| 0.575 | $-119.49 \%$ | $11.66 \%$ |
| -1.925 | $-46.83 \%$ | $-42.33 \%$ |
| -0.659 | $-11.41 \%$ | $-16.98 \%$ |
| 9.314 | $46.66 \%$ | $341.19 \%$ |
| 1.295 | $-76.85 \%$ | $31.11 \%$ |
| -3.129 | $-102.12 \%$ | $-71.62 \%$ |
| -1.316 | $-68.89 \%$ | $-37.63 \%$ |
| -1.973 | $-64.76 \%$ | $-62.84 \%$ |
| -1.232 | $-58.33 \%$ | $-34.55 \%$ |
| -5.568 | $-14.87 \%$ | $-132.49 \%$ |
| -1.259 | $45.20 \%$ | $-35.44 \%$ |
| 1.000 | $127.71 \%$ | $30.86 \%$ |
| -3.083 | $-34.91 \%$ | $-78.57 \%$ |
| -0.946 | $-64.09 \%$ | $-25.29 \%$ |
| -2.566 | $-58.59 \%$ | $-73.40 \%$ |
| -2.886 | $-44.98 \%$ | $-81.11 \%$ |
| -1.089 | $-47.53 \%$ | $-30.62 \%$ |
| -1.209 | $-41.52 \%$ | $-42.58 \%$ |
| -2.263 | $-71.75 \%$ | $-63.14 \%$ |
| -2.030 | $-20.77 \%$ | $-55.27 \%$ |
| 1.601 | $-53.06 \%$ | $46.25 \%$ |
| -0.443 | $-29.98 \%$ | $-13.16 \%$ |
| -2.608 | $-95.41 \%$ | $-77.40 \%$ |
| -0.293 | $49.23 \%$ | $-12.36 \%$ |
| 1.317 | $-22.71 \%$ | $39.90 \%$ |
| -2.249 | $-5.99 \%$ | $-65.32 \%$ |
| 0.919 | $-9.62 \%$ | $37.87 \%$ |
| -1.969 | $-103.09 \%$ | $-57.05 \%$ |
| -2.634 | $-70.91 \%$ | $-76.62 \%$ |
| -2.736 | $-68.88 \%$ | $-85.37 \%$ |
| -3.377 | $-63.35 \%$ | $-115.26 \%$ |
| -2.307 | $-57.49 \%$ | $-65.51 \%$ |
| -2.050 | $-48.34 \%$ | $-74.00 \%$ |
| -0.984 | $-50.91 \%$ | $-33.06 \%$ |
| -1.524 | $-21.91 \%$ | $-48.51 \%$ |
| -1.532 | $-52.28 \%$ | $-46.97 \%$ |
| -0.778 | $-19.44 \%$ | $-25.73 \%$ |
| 2.462 | $42.97 \%$ | $91.88 \%$ |


| -2.227 | $-82.59 \%$ | $-70.31 \%$ |
| ---: | ---: | ---: |
| -0.026 | $6.83 \%$ | $-0.93 \%$ |
| -3.307 | $-92.99 \%$ | $-105.09 \%$ |
| -2.604 | $-69.08 \%$ | $-82.71 \%$ |
| -2.553 | $-93.34 \%$ | $-80.05 \%$ |
| -2.311 | $-88.68 \%$ | $-79.22 \%$ |
| -2.201 | $-90.20 \%$ | $-67.21 \%$ |
| -1.094 | $-60.67 \%$ | $-36.84 \%$ |
| -1.454 | $-53.70 \%$ | $-55.36 \%$ |
| -0.686 | $38.01 \%$ | $-28.98 \%$ |
| -3.263 | $-109.14 \%$ | $-118.49 \%$ |
| -0.682 | $65.89 \%$ | $-24.04 \%$ |
| 1.585 | $36.16 \%$ | $56.41 \%$ |
| -1.240 | $-51.69 \%$ | $-46.93 \%$ |
| -2.680 | $-84.52 \%$ | $-104.03 \%$ |
| -0.786 | $-18.52 \%$ | $-33.38 \%$ |
| -2.706 | $-106.50 \%$ | $-90.10 \%$ |
| -2.069 | $49.00 \%$ | $-68.90 \%$ |
| -2.225 | $-93.56 \%$ | $-91.85 \%$ |
| -1.214 | $52.78 \%$ | $-41.31 \%$ |
| -1.192 | $-47.41 \%$ | $-42.66 \%$ |
| 0.337 | $11.28 \%$ | $12.81 \%$ |
| -1.031 | $89.30 \%$ | $-52.26 \%$ |
| -0.814 | $-16.65 \%$ | $-30.76 \%$ |
| -1.264 | $-103.16 \%$ | $-49.30 \%$ |
| -0.207 | $-67.55 \%$ | $-8.11 \%$ |
| -1.908 | $-38.73 \%$ | $-81.04 \%$ |
| -2.123 | $-81.15 \%$ | $-78.37 \%$ |
| -2.050 | $-83.41 \%$ | $-72.26 \%$ |
| -2.565 | $-151.36 \%$ | $-133.22 \%$ |
| 0.736 | $-14.01 \%$ | $28.38 \%$ |
| -0.464 | $-103.62 \%$ | $-17.84 \%$ |
| -2.073 | $-34.55 \%$ | $-86.37 \%$ |
| -2.584 | $-67.18 \%$ | $-93.20 \%$ |
| 1.779 | $6.63 \%$ | $87.09 \%$ |
| -1.187 | $-47.20 \%$ | $-53.60 \%$ |
| 1.837 | $128.60 \%$ | $116.15 \%$ |
| -0.569 | $-71.38 \%$ | $-25.64 \%$ |
| -2.056 | $-88.95 \%$ | $-79.27 \%$ |
| 0.256 | $-51.13 \%$ | $10.70 \%$ |
| -1.748 | $-99.88 \%$ | $-76.60 \%$ |
| 0.688 | $10.57 \%$ | $30.80 \%$ |
|  |  |  |


| 0.057 | $7.18 \%$ | $2.51 \%$ |
| ---: | ---: | ---: |
| -2.060 | $16.72 \%$ | $-89.90 \%$ |
| 0.005 | $-52.08 \%$ | $0.18 \%$ |
| -1.027 | $-114.61 \%$ | $-44.50 \%$ |
| -0.627 | $8.97 \%$ | $-28.16 \%$ |
| -0.858 | $4.72 \%$ | $-35.77 \%$ |
| -1.682 | $22.42 \%$ | $-74.56 \%$ |
| -0.341 | $-23.75 \%$ | $-14.41 \%$ |
| 0.686 | $-80.62 \%$ | $26.28 \%$ |
| -1.448 | $-79.95 \%$ | $-55.77 \%$ |
| -1.607 | $-59.72 \%$ | $-69.58 \%$ |
| -0.587 | $-110.25 \%$ | $-27.04 \%$ |
| 0.261 | $-48.12 \%$ | $11.47 \%$ |
| -1.585 | $-16.74 \%$ | $-66.15 \%$ |
| 1.633 | $130.07 \%$ | $79.33 \%$ |
| -1.392 | $46.21 \%$ | $-58.74 \%$ |
| -2.171 | $-15.67 \%$ | $-89.69 \%$ |
| -0.780 | $70.82 \%$ | $-33.74 \%$ |
| 0.355 | $189.90 \%$ | $23.88 \%$ |
| -1.202 | $2.92 \%$ | $-52.69 \%$ |
| -0.828 | $34.96 \%$ | $-43.09 \%$ |
| -1.340 | $-73.40 \%$ | $-69.47 \%$ |
| 0.279 | $-48.09 \%$ | $15.49 \%$ |
| 1.285 | $-35.95 \%$ | $68.84 \%$ |
| -2.462 | $-117.37 \%$ | $-106.05 \%$ |
| 0.712 | $93.38 \%$ | $46.03 \%$ |
| -1.458 | $-48.02 \%$ | $-62.99 \%$ |
| -1.612 | $-9.56 \%$ | $-74.54 \%$ |
| -2.819 | $-114.97 \%$ | $-130.17 \%$ |
| 0.780 | $18.27 \%$ | $42.66 \%$ |
| -1.476 | $-124.15 \%$ | $-68.71 \%$ |
| -1.874 | $-46.08 \%$ | $-82.18 \%$ |
| 0.116 | $-62.62 \%$ | $5.09 \%$ |
| -0.815 | $182.87 \%$ | $-40.91 \%$ |
| -0.258 | $12.69 \%$ | $-12.29 \%$ |
| 1.565 | $-78.24 \%$ | $80.04 \%$ |
| -0.652 | $-82.14 \%$ | $-33.84 \%$ |
| -0.238 | $15.63 \%$ | $-10.92 \%$ |
| -0.667 | $57.13 \%$ | $-37.97 \%$ |
| 2.348 | $-83.48 \%$ | $162.80 \%$ |
| 3.042 | $201.62 \%$ | $220.54 \%$ |
| 0.420 | $-76.83 \%$ | $26.91 \%$ |
|  |  |  |


| 0.552 | $-46.24 \%$ | $27.44 \%$ |
| ---: | ---: | ---: |
| -0.481 | $-124.41 \%$ | $-25.24 \%$ |
| 1.043 | $-2.52 \%$ | $53.52 \%$ |
| 0.918 | $-19.12 \%$ | $65.10 \%$ |
| -2.031 | $-61.68 \%$ | $-99.68 \%$ |
| -1.474 | $-84.48 \%$ | $-72.77 \%$ |
| -1.273 | $-72.98 \%$ | $-63.15 \%$ |
| 0.091 | $-35.02 \%$ | $4.87 \%$ |
| -1.245 | $-82.59 \%$ | $-61.61 \%$ |
| 0.160 | $-42.10 \%$ | $10.91 \%$ |
| -1.499 | $69.49 \%$ | $-77.04 \%$ |
| -0.060 | $-86.37 \%$ | $-2.83 \%$ |
| -1.636 | $-109.13 \%$ | $-79.28 \%$ |
| -1.264 | $4.22 \%$ | $-63.09 \%$ |
| 0.628 | $63.45 \%$ | $36.10 \%$ |
| 2.112 | $55.89 \%$ | $129.23 \%$ |
| -0.085 | $-26.45 \%$ | $-4.57 \%$ |
| -0.011 | $-36.40 \%$ | $-0.70 \%$ |
| -0.273 | $25.54 \%$ | $-14.73 \%$ |
| 0.862 | $70.13 \%$ | $52.57 \%$ |
| 2.121 | $7.18 \%$ | $117.11 \%$ |
| 1.743 | $187.58 \%$ | $84.07 \%$ |
| 2.948 | $6.64 \%$ | $173.73 \%$ |
| 0.640 | $-10.15 \%$ | $42.89 \%$ |
| -1.576 | $-56.75 \%$ | $-76.36 \%$ |
| 0.574 | $62.32 \%$ | $35.27 \%$ |
| 1.201 | $127.92 \%$ | $65.09 \%$ |
| -0.469 | $-83.59 \%$ | $-22.83 \%$ |
| -0.450 | $-9.13 \%$ | $-26.57 \%$ |
| 0.361 | $-111.71 \%$ | $17.65 \%$ |
| -0.192 | $-52.80 \%$ | $-11.63 \%$ |
| 0.900 | $-53.96 \%$ | $56.94 \%$ |
| 0.629 | $4.24 \%$ | $31.67 \%$ |
| 1.293 | $-2.23 \%$ | $65.25 \%$ |
| -0.872 | $48.32 \%$ | $-60.37 \%$ |
| -0.178 | $-67.97 \%$ | $-9.50 \%$ |
| 1.945 | $-45.94 \%$ | $98.61 \%$ |
| -1.099 | $47.44 \%$ | $-72.98 \%$ |
| -1.044 | $-52.24 \%$ | $-54.65 \%$ |
| -1.267 | $-90.31 \%$ | $-64.96 \%$ |
| -0.266 | $86.23 \%$ | $-15.05 \%$ |
| -0.331 | $13.71 \%$ | $-19.68 \%$ |
|  |  |  |


| -0.609 | $-65.54 \%$ | $-36.62 \%$ |
| ---: | ---: | ---: |
| -1.315 | $-92.73 \%$ | $-69.21 \%$ |
| 2.550 | $21.49 \%$ | $170.46 \%$ |
| -1.079 | $326.91 \%$ | $-67.68 \%$ |
| 1.486 | $47.36 \%$ | $88.24 \%$ |
| -0.384 | $-12.20 \%$ | $-24.61 \%$ |
| -1.066 | $15.69 \%$ | $-70.42 \%$ |
| -0.355 | $25.25 \%$ | $-25.64 \%$ |
| -0.927 | $-83.37 \%$ | $-58.66 \%$ |
| -1.111 | $-51.90 \%$ | $-64.14 \%$ |
| -0.569 | $15.32 \%$ | $-30.95 \%$ |
| 0.517 | $-34.86 \%$ | $31.71 \%$ |
| -1.318 | $-52.88 \%$ | $-72.29 \%$ |
| 2.318 | $-180.67 \%$ | $155.90 \%$ |
| -0.879 | $-118.48 \%$ | $-64.98 \%$ |
| -0.604 | $-30.56 \%$ | $-42.89 \%$ |
| 0.597 | $2.11 \%$ | $38.81 \%$ |
| -1.175 | $-66.34 \%$ | $-73.02 \%$ |
| 0.065 | $32.78 \%$ | $4.88 \%$ |
| 3.440 | $18.64 \%$ | $282.95 \%$ |
| 0.537 | $-105.52 \%$ | $33.30 \%$ |
| -0.413 | $-881.91 \%$ | $46.62 \%$ |
| 0.766 | $-9.67 \%$ | $46.77 \%$ |
| 1.215 | $41.20 \%$ | $94.95 \%$ |
| -0.226 | $-22.41 \%$ | $-15.28 \%$ |
| -0.192 | $-71.50 \%$ | $-12.73 \%$ |
| -1.393 | $237.50 \%$ | $-91.44 \%$ |
| -0.309 | $-75.98 \%$ | $-20.61 \%$ |
| -0.003 | $-37.42 \%$ | $-0.18 \%$ |
| -0.128 | $-102.26 \%$ | $-8.68 \%$ |
| -1.330 | $-124.87 \%$ | $-80.94 \%$ |
| 1.265 | $21.49 \%$ | $94.32 \%$ |
| 0.183 | $-35.71 \%$ | $12.87 \%$ |
| 0.494 | $-16.75 \%$ | $33.33 \%$ |
| -0.271 | $-103.29 \%$ | $-22.63 \%$ |
| -0.561 | $1.93 \%$ | $-41.44 \%$ |
| 0.239 | $-67.97 \%$ | $14.35 \%$ |
| -1.825 | $-80.11 \%$ | $-118.95 \%$ |
| -0.404 | $-62.92 \%$ | $-27.50 \%$ |
| -1.309 | $38.79 \%$ | $-79.11 \%$ |
| -1.128 | $-84.95 \%$ | $-77.30 \%$ |
| 1.210 | $-56.63 \%$ | $73.51 \%$ |
|  |  |  |


| 1.530 | $23.41 \%$ | $106.41 \%$ |
| ---: | ---: | ---: |
| -1.681 | $-68.77 \%$ | $-126.98 \%$ |
| -1.120 | $16.63 \%$ | $-86.85 \%$ |
| 0.140 | $-32.12 \%$ | $9.87 \%$ |
| -0.692 | $12.08 \%$ | $-45.85 \%$ |
| -0.143 | $-7.33 \%$ | $-10.44 \%$ |
| -0.388 | $-47.14 \%$ | $-25.48 \%$ |
| -0.282 | $-33.92 \%$ | $-19.95 \%$ |
| 0.997 | $-42.73 \%$ | $72.83 \%$ |
| 0.866 | $118.57 \%$ | $73.62 \%$ |
| -1.242 | $-82.42 \%$ | $-90.96 \%$ |
| 1.210 | $-9.04 \%$ | $86.53 \%$ |
| -1.239 | $30.11 \%$ | $-85.32 \%$ |
| 0.300 | $-112.25 \%$ | $23.06 \%$ |
| 0.423 | $-79.23 \%$ | $26.61 \%$ |
| -0.126 | $-57.92 \%$ | $-8.90 \%$ |
| -0.224 | $-79.63 \%$ | $-14.10 \%$ |
| -0.275 | $-26.26 \%$ | $-21.80 \%$ |
| -1.539 | $20.06 \%$ | $-97.56 \%$ |
| 1.291 | $-26.21 \%$ | $91.72 \%$ |
| 0.220 | $-50.36 \%$ | $16.04 \%$ |
| -0.210 | $-68.25 \%$ | $-14.11 \%$ |
| 3.959 | $92.69 \%$ | $277.97 \%$ |
| -0.838 | $-72.85 \%$ | $-57.16 \%$ |
| 0.024 | $156.45 \%$ | $7.23 \%$ |
| 0.202 | $-67.81 \%$ | $15.40 \%$ |
| -0.286 | $-62.15 \%$ | $-33.58 \%$ |
| -0.315 | $19.27 \%$ | $-22.30 \%$ |
| 0.360 | $-48.64 \%$ | $25.53 \%$ |
| -0.700 | $216.65 \%$ | $-45.24 \%$ |
| 0.168 | $-7.70 \%$ | $15.93 \%$ |
| 0.234 | $-14.51 \%$ | $16.48 \%$ |
| -0.483 | $-35.66 \%$ | $-32.16 \%$ |
| 1.073 | $-63.90 \%$ | $69.77 \%$ |
| 0.085 | $100.77 \%$ | $7.91 \%$ |
| -0.030 | $-24.66 \%$ | $-2.35 \%$ |
| 0.993 | $60.40 \%$ | $77.27 \%$ |
| -1.134 | $-72.19 \%$ | $-79.00 \%$ |
| 0.735 | $19.84 \%$ | $66.30 \%$ |
| -0.930 | $-66.05 \%$ | $-67.28 \%$ |
| 0.535 | $-19.80 \%$ | $42.17 \%$ |
| 0.027 | $62.86 \%$ | $2.25 \%$ |
|  |  |  |


| 0.867 | $-37.07 \%$ | $70.21 \%$ |
| ---: | ---: | ---: |
| -1.637 | $-94.03 \%$ | $-114.31 \%$ |
| -0.770 | $-22.92 \%$ | $-56.94 \%$ |
| 2.027 | $133.80 \%$ | $134.76 \%$ |
| 0.061 | $97.63 \%$ | $4.79 \%$ |
| -1.342 | $-44.06 \%$ | $-89.50 \%$ |
| 0.494 | $120.28 \%$ | $36.23 \%$ |
| 0.514 | $-15.35 \%$ | $47.78 \%$ |
| -0.505 | $-54.35 \%$ | $-36.97 \%$ |
| -0.158 | $-43.24 \%$ | $-11.13 \%$ |
| -0.948 | $-86.52 \%$ | $-83.38 \%$ |
| -0.473 | $-80.54 \%$ | $-32.19 \%$ |
| 1.195 | $41.55 \%$ | $88.63 \%$ |
| -0.926 | $-27.41 \%$ | $-66.02 \%$ |
| -0.584 | $-72.59 \%$ | $-43.72 \%$ |
| 1.006 | $-37.28 \%$ | $84.02 \%$ |
| -1.382 | $59.09 \%$ | $-101.84 \%$ |
| -0.223 | $-47.44 \%$ | $-15.33 \%$ |
| 1.396 | $-37.07 \%$ | $117.37 \%$ |
| -0.184 | $25.88 \%$ | $-12.68 \%$ |
| 0.753 | $-46.29 \%$ | $58.13 \%$ |
| -0.388 | $-36.60 \%$ | $-28.33 \%$ |
| 0.870 | $-49.53 \%$ | $73.47 \%$ |
| 2.182 | $197.25 \%$ | $576.28 \%$ |
| 0.642 | $-93.45 \%$ | $54.50 \%$ |
| 0.787 | $-33.06 \%$ | $61.95 \%$ |
| -0.340 | $-32.24 \%$ | $-31.73 \%$ |
| 0.556 | $-15.05 \%$ | $41.43 \%$ |
| -1.088 | $-1.93 \%$ | $-87.92 \%$ |
| 1.542 | $90.29 \%$ | $137.03 \%$ |
| -2.336 | $58.69 \%$ | $-164.00 \%$ |
| 0.636 | $-120.23 \%$ | $77.32 \%$ |
| -0.603 | $-41.93 \%$ | $-44.91 \%$ |
| 1.445 | $-7.27 \%$ | $110.57 \%$ |
| 0.664 | $-28.01 \%$ | $47.03 \%$ |
| 1.877 | $147.37 \%$ | $152.73 \%$ |
| -0.993 | $15.37 \%$ | $-81.12 \%$ |
| 0.318 | $44.70 \%$ | $34.44 \%$ |
| 0.635 | $207.98 \%$ | $70.37 \%$ |
| 0.533 | $-22.07 \%$ | $38.36 \%$ |
| 0.259 | $-51.01 \%$ | $20.28 \%$ |
| -0.206 | $-18.49 \%$ | $-18.15 \%$ |
|  |  |  |


| 1.520 | $-157.06 \%$ | $147.20 \%$ |
| ---: | ---: | ---: |
| 1.542 | $-54.88 \%$ | $112.22 \%$ |
| 0.137 | $4.32 \%$ | $12.10 \%$ |
| -0.860 | $-113.60 \%$ | $-69.44 \%$ |
| -0.822 | $-61.30 \%$ | $-64.99 \%$ |
| 0.034 | $-59.61 \%$ | $2.83 \%$ |
| 0.869 | $-83.36 \%$ | $73.69 \%$ |
| -0.696 | $95.84 \%$ | $-51.62 \%$ |
| 2.025 | $209.66 \%$ | $178.80 \%$ |
| 0.634 | $325.08 \%$ | $60.19 \%$ |
| 0.092 | $-61.54 \%$ | $9.01 \%$ |
| 0.987 | $151.47 \%$ | $201.65 \%$ |
| -0.294 | $-40.78 \%$ | $-27.38 \%$ |
| 0.583 | $-50.50 \%$ | $50.91 \%$ |
| 0.702 | $44.60 \%$ | $71.86 \%$ |
| -0.375 | $37.52 \%$ | $-30.88 \%$ |
| 1.116 | $-1.00 \%$ | $98.61 \%$ |
| -0.520 | $-138.52 \%$ | $-59.01 \%$ |
| -0.250 | $-69.75 \%$ | $-21.03 \%$ |
| 0.062 | $13.23 \%$ | $6.53 \%$ |
| -0.868 | $14.61 \%$ | $-80.85 \%$ |
| 0.784 | $-69.31 \%$ | $68.88 \%$ |
| -0.465 | $-72.08 \%$ | $-38.81 \%$ |
| 0.357 | $47.58 \%$ | $31.50 \%$ |
| 0.889 | $-119.86 \%$ | $78.41 \%$ |
| 1.250 | $165.36 \%$ | $188.15 \%$ |
| -0.653 | $-9.24 \%$ | $-60.79 \%$ |
| 0.075 | $44.27 \%$ | $6.79 \%$ |
| -0.267 | $37.70 \%$ | $-27.80 \%$ |
| -0.043 | $-25.97 \%$ | $-3.88 \%$ |
| -0.982 | $-72.91 \%$ | $-84.21 \%$ |
| -1.263 | $-114.16 \%$ | $-134.08 \%$ |
| 1.712 | $-61.89 \%$ | $174.41 \%$ |
| 0.458 | $91.07 \%$ | $48.89 \%$ |
| -0.451 | $-0.70 \%$ | $-47.12 \%$ |
| -0.416 | $-9.13 \%$ | $-39.50 \%$ |
| 0.190 | $46.81 \%$ | $19.48 \%$ |
| -0.501 | $-40.78 \%$ | $-46.02 \%$ |
| 0.694 | $67.14 \%$ | $71.68 \%$ |
| 0.902 | $-35.07 \%$ | $73.51 \%$ |
| 0.228 | $-94.12 \%$ | $19.66 \%$ |
| -0.731 | $-47.90 \%$ | $-78.43 \%$ |
|  |  |  |


| 0.188 | $-47.66 \%$ | $17.70 \%$ |
| ---: | ---: | ---: |
| 1.335 | $-145.27 \%$ | $140.28 \%$ |
| -0.090 | $-70.19 \%$ | $-7.88 \%$ |
| -0.672 | $430.14 \%$ | $-107.32 \%$ |
| 0.319 | $-128.35 \%$ | $26.89 \%$ |
| -0.353 | $-25.07 \%$ | $-35.36 \%$ |
| 2.073 | $124.71 \%$ | $175.17 \%$ |
| 1.827 | $-9.32 \%$ | $176.90 \%$ |
| -0.577 | $-19.70 \%$ | $-53.42 \%$ |
| -0.742 | $-61.71 \%$ | $-67.22 \%$ |
| -0.851 | $-62.57 \%$ | $-84.11 \%$ |
| 1.565 | $-78.44 \%$ | $134.43 \%$ |
| 1.384 | $252.32 \%$ | $207.14 \%$ |
| 1.652 | $-48.02 \%$ | $248.30 \%$ |
| 1.194 | $73.05 \%$ | $119.25 \%$ |
| -0.769 | $-121.09 \%$ | $-81.16 \%$ |
| 1.647 | $181.08 \%$ | $182.30 \%$ |
| -0.883 | $-2.56 \%$ | $-81.97 \%$ |
| 0.718 | $108.84 \%$ | $62.96 \%$ |
| 0.821 | $88.37 \%$ | $81.71 \%$ |
| 0.664 | $-27.62 \%$ | $58.61 \%$ |
| -0.417 | $-81.39 \%$ | $-40.44 \%$ |
| 1.389 | $44.28 \%$ | $165.45 \%$ |
| -0.067 | $-46.62 \%$ | $-7.78 \%$ |
| 0.138 | $-21.38 \%$ | $14.28 \%$ |
| -0.568 | $-91.98 \%$ | $-55.16 \%$ |
| -0.341 | $23.68 \%$ | $-35.56 \%$ |
| -0.739 | $98.36 \%$ | $-67.29 \%$ |
| 0.251 | $208.00 \%$ | $30.66 \%$ |
| -0.731 | $-29.00 \%$ | $-71.75 \%$ |
| 0.376 | $-39.30 \%$ | $38.47 \%$ |
| -1.183 | $28.91 \%$ | $-108.80 \%$ |
| 2.127 | $1568.35 \%$ | $931.81 \%$ |
| 0.974 | $79.89 \%$ | $89.68 \%$ |
| -0.140 | $-70.93 \%$ | $-12.91 \%$ |
| -0.427 | $-126.39 \%$ | $-42.99 \%$ |
| -0.054 | $17.78 \%$ | $-6.44 \%$ |
| -0.406 | $87.04 \%$ | $-38.42 \%$ |
| -0.600 | $-121.77 \%$ | $-64.20 \%$ |
| 2.179 | $199.61 \%$ | $206.78 \%$ |
| 1.160 | $111.86 \%$ | $110.75 \%$ |
| -0.736 | $81.20 \%$ | $-79.11 \%$ |
|  |  |  |


| 0.158 | $25.61 \%$ | $18.18 \%$ |
| ---: | ---: | ---: |
| 0.001 | $35.83 \%$ | $0.19 \%$ |
| -0.310 | $-11.26 \%$ | $-34.49 \%$ |
| 0.205 | $188.44 \%$ | $23.73 \%$ |
| 2.458 | $-197.82 \%$ | $239.77 \%$ |
| 0.090 | $-99.60 \%$ | $8.86 \%$ |
| 0.572 | $-64.40 \%$ | $77.28 \%$ |
| 0.074 | $-269.24 \%$ | $13.90 \%$ |
| 0.415 | $22.15 \%$ | $44.76 \%$ |
| 3.690 | $173.75 \%$ | $997.89 \%$ |
| 0.409 | $-207.21 \%$ | $40.74 \%$ |
| 0.473 | $-63.73 \%$ | $51.89 \%$ |
| -1.058 | $129.43 \%$ | $-119.43 \%$ |

## Supplemental Note 1

## Systematic dissection of a previously cloned cenRNA\#1

We previously used a conventional TOPO T/A cloning strategy in an initial attempt to identify small centromeric RNAs, from which one centromeric long non-coding RNA (cenRNA\#1) was isolated and cloned from CENP-A associated chromatin (1). This approach yielded a putative fragment of 675 bases of an unmappable sequence. Despite numerous experimental attempts, we were unable to identify a human genomic origin for cenRNA\#1. Analysis of this sequence showed that it had extensive repeat structure and the absence of significant sequence similarity to the human reference genome. Both of these qualities were not surprising in a transcript arising from the centromere, which is also repetitive and incompletely represented in the reference genome. Nonetheless, to query non-reference origins of this sequence, we performed additional alignments spanning multiple sequence databases and published sequences (Supplemental Note - Table 1 and Supplemental Note - Table 2). Additionally, to improve the accuracy of the cenRNA\#1 sequence, we re-sequenced 6 clones of cenRNA\#1which led to the rescue of 12 N 's and 27 base calls changed (Supplemental Note - Figure 1).

Again, BLAST alignment to public human genome reference data, to human transcript sequences, and to compiled $\alpha$-satellite monomers and novel repeating centromeric elements from the literature yielded no significant alignments (Supplemental Note - Table 1) (2-4). Because of this lack of similarity to human sequence, we performed additional screens against multiple specialized databases for technical artifact (VecScreen, http://www.ncbi.nlm.nih.gov/VecScreen/VecScreen.html), for contamination from exogenous sequence (nr database), from small RNAs and from viral sequences (Supplemental Note - Table 1). None of these searches yielded a significant result. We hypothesized cenRNA\#1 was unique to HeLa cells (the cell line used in the previous work) and may have derived from a region of re-arrangement or chromothripsis. However, after permission received from the NIH HeLa Genome Data Access Working Group, no evidence of homology to cenRNA\#1was found in the sequenced $\operatorname{HeLa} \operatorname{strain}(5,6)$.

Next, we hypothesized that cenRNA\#1 might be a composite of spliced RNAs. Indeed, progress was made in identifying cenRNA\#1 when we searched patent databases in the European Nucleotide Archive, which indexes sequences cited in U.S. patent applications, including primers and adapters not indexed and searchable at GenBank $(7,8)$. This led to the discovery that cenRNA\#1 is largely composed of sequence identical to adapters used in our RNA cloning approach and described in Pfeffer et al. (Supplemental Note - Figure 2; (1,9)). We identified three regions in cenRNA\#1 that did not overlap contiguous, full-length sequences in (9). Although these regions contain partial matches to these sequences, we compared sequence identity with their respective best hits in the human genome, to weigh the evidence for a transcript origin of these regions. The human genome hits did not occur in centromeres (Supplemental Note - Table 2 and Supplemental Note - Table 3). In our initial analysis of cenRNA\#1, we examined the ordered pattern of repeats in the light of $\alpha$-satellite structure. We identified a 28bp repeat element regularly spaced and displaying a weak similar to the CENP-B box (57\%), suggesting some variant of $\alpha$-satellite structure. The same analysis with the re-sequenced cenRNA\#1 shows that this original 28bp repeat is present within two adapter sequences, and has modest homology to the inner kinetochore protein CENPB box (52\%) (Supplemental Note - Table 4).

Two shRNAs were generated from this cenRNA\#1 sequence and led to cell division defects (1). Based on the resequencing results, three base calls within each shRNA were changed, which removes their uniqueness within cenRNA\#1 and lead to their similarity over 26/29 bases (Supplemental Note - Table 5). Neither shRNA had a
significant match to the human genome or known transcripts. However, the best hit is to a lncRNA on chromosome 3 ( $15 / 29$ bases), proximal to the centromere, but not in the pericentromere (Supplemental Note Table 6). Surprisingly, an independent reproduction of the down-regulation of cenRNA\#1 by shRNA approach yielded the same chromosome defect as before (1), suggesting a potential function of this sequence containing lncRNA on chromosome segregation.

Supplemental Note - Table 1: Best alignment hits for cenRNA\#1 regions without contiguous full-length adapter sequences.

| Method | Database | Results |
| :--- | :--- | :--- |
| BLAST <br> alignment | Human genome reference hg19 | No significant alignment : Shorter contiguous hit (20bp) <br> than the longest contiguous hit in a random sequence of the <br> same length and GC content (23bp) |
| BLAST <br> alignment | Human transcript sequence | No significant alignment : With an average exon size of <br> 123 bases (Scherer, 2008), unlike cenRNA\#1 transcription <br> from short exons separated by long introns |
| BLAST <br> alignment | extended higher-order repeats <br> from chromosome X from (2) | No significant alignment |
| BLAST <br> alignment | hg38 reference assembly, <br> incorporating <br> megabases of new centromeric <br> assembly <br> (https://genomereference.org) | No significant alignment |
| BLAST <br> alignment | $\alpha$-satellite monomers and novel <br> repeating centromeric elements <br> from (3) | No significant alignment |
| BLAST <br> alignment | $\alpha-$-satellite monomers and novel <br> repeating centromeric elements <br> from (4) | No significant alignment |
| BLAST <br> alignment <br> alignment <br> alignment <br> alignment | VecScreen <br> nr database <br> small RNAs | Some similarities with vector sequence |
| BLAST | viral sequences | No significant alignment |


| NCBI databases | -Human genome + transcript (Build 38) <br> -Non-redundant nucleotide collection (nr/nt) <br> -Expressed sequence tags (EST) <br> -Genomic survey sequences (gss) <br> -High-throughput genomic sequences (hgts) <br> -Whole genome shotgun contigs (wgs) <br> -Transcriptome shotgun assembly seqs (TSA) |
| :---: | :---: |
| SRA studies | -DRX000595: HeLa.Std.5000ng.1st DRP000372 • Unamplified Cap Analysis of Gene Expression on a single molecule sequencer (HeliScopeCAGE) <br> -DRX001262: Hela cells (without wild-type U2AF35 induction by doxycycline) DRP000527 • RNA sequencing of wild-type or mutant U2AF35 transduced HeLa Cells <br> -DRX002709: Chromatin immunoprecipitated DNA of CFIm68 in control Hela cells DRP000897 • Illumina sequencing of CFIm68 binding regions in Hela cells <br> -DRX002710: Input DNA for CFIm68 ChIP of control Hela cells DRP000897• Illumina sequencing of CFIm68 binding regions in Hela cells <br> -DRX013196: HeLa PolII DRP001297 • Construction of Mate Pair Full-length cDNAs Libraries and Characterization of Transcriptional Start Sites and Termination Sites <br> -ERX634046: CLIP-Seq of $H$. sapiens HeLa cells to investigate transcriptome-wide mapping of PTB / hnRNP I CLIP-Seq of H. sapiens HeLa cells to investigate transcriptome-wide mapping of PTB / hnRNP I <br> -SRX749241: RnaSeq_HeLa_cell_RNaseRSRP049453 • Homo sapiens Transcriptome or Gene expression <br> -SRX749316: RnaSeq_HeLa_cell_RibominusSRP049453 • Homo sapiens Transcriptome or Gene expression <br> -ERX615573: Whole Genome Sequencing of human |


|  | -SRX699196: whole genome sequence of HeLa cells: Sample JR6- <br> UPL_ACTTGAStudy summary: SRP046745 • HeLa Genome <br> sequencing <br> -SRX699188: whole genome sequence of HeLa cells: Sample JR5- <br> QPCR_CGTACG SRP046745 • HeLa Genome sequencing |
| :--- | :--- |
| dbGaP | -Epigenetic Profiling of Human Colorectal Cancer (phs000385.v1.p1) <br> -HeLa Cell Genome Sequencing Studies (phs000640.v3.p1) |
| Specialized databases | -DASHR: database of small human noncoding RNAs (Leung, 2015) <br> -deepBase v2.0 (Zhang, 2015) <br> -EMBL Rfam database (Database of RNA family domains) <br> -mIRbase <br> - -RNAcentral |

Supplemental Note - Table 3: Best alignment hits for cenRNA\#1 regions without contiguous full-length adapter sequences

| ID | Sequence | Best hits in Pfeffer's article | Best hit in human genome |
| :---: | :---: | :---: | :---: |
| Region 1: 21bp | AGCCAACGGAATTC CTTTGGC | p2 (16/16 100\%) <br> a2 (11/11 100\%) | chr10:3723839-3723855 <br> (17/17 100\%) |
| Region $2:$ 23bp | CGCGAATTCCAGCT AGTCCAGCC | $\begin{aligned} & \text { p2 (18/18, 100\%) } \\ & \text { a1 (12/12 100\%) } \end{aligned}$ | chr11:96647943-96647960 $(18 / 18,100 \%)$ chr7:131446816-131446832 $(17 / 17,100 \%)$ chrX:24111144-24111160 $(17 / 17100 \%)$ |
| Region 3: 64bp | TCAGCCAACGGAAT TCCTCACTAACCGCG AATTCCAGCTAGTC AGCCAACGGAATTC CAGCTAGT | p2 (23/23 100\%) <br> a2 (15/15 100\%) <br> multiple short hits | $\begin{aligned} & \text { chr2:22737705- } 22737730 \\ & (23 / 26,88.5 \%) \end{aligned}$ |

Supplemental Note - Table 4: Alignment of cenRNA\#1 28bp repeat to CENP-B box.

| Score: 500 | Alignment |
| :--- | :--- |
| Sequence CENP-B: 1-17 | CENP-B: CT---TCGTTGGAAA-CGGGA |
| Sequence 28bp: 1-27 | 28bp seq: CTAAAT--TT---AACCGCGA |
| Length of alignment: 21 bases | Percentage ID: 52.38 |

Supplemental Note - Table 5: Changes to cenRNA\#1 shRNA sequence.

| shRNA | Previous sequence | New sequence |
| :--- | :--- | :--- |
| shRNA-A | CAAGCTAGTCAGCCAATGC <br> AATTCCTCAT | CAAGCTAGTCAGCCAACGG <br> AATTCCTCAC |
| shRNA-B | TGCTAGACAGCCAATGCAA <br> TTCCTCATTA | AGCTAGTCAGCCAACGGAA <br> TTCCTCACTA |

Supplemental Note - Table 6: Potential targeted IncRNA by cenRNA\#1 shRNA.

| Target |  | Alignment statistics |
| :--- | :--- | :--- |
| long intergenic non-protein coding <br> (LINC00971) |  | RNA 971 |
| Query: $\quad{ }^{7}$ AGTCAGCCAACGGAA $^{21}$ |  |  |

Supplemental Note - Figure 1: Alignment of the original cenRNA1 with new sequencing results. Six clones of cenRNA\#1 were re-sequenced. Adjustment was performed when similar uncalled bases ( 12 N 's) or called bases (27) were found in the six clones ( $\sim 6 \%$ of total sequence changed).


Supplemental Note - Figure 2: Map of re-sequenced cenRNA\#1. Sequence alignments revealed that cenRNA\#1 is principally composed of adapters used for cloning step described in (9). Only full-length, $100 \%$ identical locations of Pfeffer's sequences are indicated (except at sequence ends).


## Supplemental Note - References

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## Supplemental Datafile 1: Coding potential of cenRNAs

## cenRNA\#2

\# Longest ORF
Label Strand Frame Start Stop Length (nt $\mid$ aa)
$\begin{array}{llllll}\text { ORF2 - } & 1 & 406 & 122 & 285 \mid 94\end{array}$
>lıl|ORF2
MKYQSSQTIYYILYIKYQSTQGIYSIVYKKYQSTQSMYYIPYIKYKITSNIYFILYIKYQSTPDIYTI VYIKYQSTQTIHYTLYIKYEITSNIY
\# Best TBLASTX hit (nr database)
hypothetical protein Q611_LSC00001G0001, partial [Leuconostoc sp. DORA_2]
Sequence ID: ETJ00816.1
Range 1: 1 to 95
Alignment statistics for match \#1
Score Expect Method Identities Positives Gaps
Frame
157 bits(396) 9e-52 Compositional matrix adjust. 89/95(94\%) 92/95(96\%) 0/95(0\%)
-1
Query 415 ILYMKYQSSQTIYYILYIKYQSTQGIYSIVYKKYQSTQSMYYIPYIKYKITSNIYFILYI

ILYMKYQSSQTIYYILYIKYQSTQGIYSI -YKKYQSTQSMYYI -YIKY - -TSNIYFILYI
Sbjct 1 ILYMKYQSSQTIYYILYIKYQSTQGIYSILYKKYQSTQSMYYILYIKYESTSNIYFILYI 60

Query 235 KYQSTPDIYTIVYIKYQSTQTIHYTLYIKYEITSN 131
KYQSTPDIY -IVYIKYQSTQTIHY -LYIKYEITSN
Sbjct 61 KYQSTPDIYSIVYIKYQSTQTIHYILYIKYEITSN 95

## cenRNA\#3

\# Longest ORF
[ No ORF found ]
\# Best TBLASTX hit
Uncharacterised protein [Streptococcus pneumoniae]
Sequence ID: CJS63439.1 Length: 157 Number of Matches: 4
Range 1: 45 to 154
Alignment statistics for match \#1
Score Expect Method Identities Positives Gaps
Frame
159 bits(401) 7e-48 Compositional matrix adjust. 83/110(75\%) 89/110(80\%) 0/110(0\%)
-3

Query 348
GAVIPFPTKSSERSKYPLVDSTKSVSQTCSIQRNVQLCDLNSIITKYFLRMLLSSFSMKL 169
G - -IPFPTKSSERSKYPL -DSTK -V -- -CSI - -NVQL - -LNSI -TK -FLR -L -S -F -MK -
Sbjct 45 GKLIPFPTKSSERSKYPLADSTKRVFGNCSIITNVQLSELNSIVTKNFLRVLPSGFYMKF
104

Query 168 FPLLP * ASKRSKSPLAHSTTRVFPNCSINRNVQLCEVNAIITKQFLRMLL 19
FP -LP -ASKRSKSPLA -ST -RVF -NCSI -RNVQL -E -NAIIT -QFLRMLL
Sbjct 105 FPSLPQASKRSKSPLADSTKRVFANCSIKRNVQLWELNAIITEQFLRMLL 154
cenRNA\#4
\# Longest ORF
Label Strand Frame Start Stop Length (nt $\mid a a$ )

ORF1 + 

$>\mathrm{lcl} \mid$ ORF 1
MHSQELFGDVCIQLPELNFPLERAAMKHSFSRICKWTIGGLCGLWWKRKYLHLNTREKHSQKL LCDDCIHLTELTIPIDRAVWKHSCCGMCKWRFGVL
\# Best TBLASTX hit (nr database)
hypothetical protein POVWA2_087530 [Plasmodium ovale wallikeri]
Sequence ID: SBT58769.1Length: 271Number of Matches: 8
Range 1: 5 to $258 \backslash$

Alignment statistics for match \#1
Score Expect Method Identities Positives Gaps
Frame
251 bits(641) 2e-79 Compositional matrix adjust. 152/259(59\%) 171/259(66\%) 28/259(10\%) -3

Query 714 KEVSENASV * LGAVIPFPTKSSERSKYPLADSTKSVI--------------QTCSI----- 589

+ ESEASVL + IPF T SS+RSKYPLAD T+S + TCS
Sbjct 5 QEDSETASVYLAEIIPFATNSSDRSKYPLADCTESEVISFTTIGLKEVQLSTCSFYKKSV 64

Query 588 -----QRNVQLCELNSIITKYFLRMLLSSFSMKLFPLLP*ASKHSKSPLAHSTTRVFPNC 424

QR VQ C LN+ ITK LRMLL S S++ P +S+ K PLA T VFPNC
Sbjct 65 SNLNYQRKVQHCGLNANITKKVLRMLLFSSVRFIPFPTKSSERPKYPLADPTDSVFPNC 123

Query 423
SINRNGQLCEVNAIITKQFLRMLLSSI*VKIFPFPPQTTKPSNRPLADSRKRVFHSCSFQ 244
SI RN Q CE+N++ FLRM LSS KI PFPPQ +KPS PLADSRKRVF S S +
Sbjct 124 SIQRNVQPCELNSV----FLRMHLSSSYGKIIPFPPQASKPSKYPLADSRKRVFQSFSLK 179

Query 243
RKVQLWELNTNITKKFLRMHLYSFYVKMIPFPTKSSKRSTCPLADATEREFQNCALKRSV 64 RKVQL EL NITKKFLRM L+SF VK+IPFPTKSSKR PLADATER F NC LKR++

Sbjct 180
RKVQLCELKANITKKFLRMLLFSFSVKIIPFPTKSSKRPKHPLADATERVFGNCCLKRNL 239

Query 63 QLRELNAVITEKLLRMLLS 7 QL ELNAVIT K L MLLS

Sbjct 240 QLCELNAVITNKFLTMLLS 258

