CENP-A associated lncRNAs influence chromosome segregation in human cells

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ABSTRACT

Transcription occurs ubiquitously throughout non-coding parts of the genome, including at repetitive α-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 171bp monomer α-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 α-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, over-expression or down-regulation of centromeric α-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 Mis18α (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 ~1.3kb 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 α-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 CENP-A 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 α-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 ~1kb 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°C, 5% 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 (0.5mM, #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 125mM glycine (#50046, Sigma-Aldrich). Then, nuclei were isolated in TM2 buffer (20mM Tris–HCl, pH 8.0 (#15568-025, Thermo Fisher Scientific); 2mM $MgCl_2$ (#AM9530G, Thermo Fisher Scientific); 0.5mM PMSF (#78830, Sigma-Aldrich); 1X complete protease inhibitor cocktail (#05892953001, Roche, Indianapolis, IN) complemented with 0.5% Nonidet^{TM} P40 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 10mM RVC. Chromatin was MNase-digested (MNase, #N3755, Sigma-Aldrich) in 0.1M TE buffer (0.1M NaCl (#24740-011, Thermo Fisher Scientific); 10mM Tris–HCl, pH 8.0; 0.2mM EGTA (#03777, Sigma-Aldrich) in presence of 2mM $CaCl_2$ (#746495, Sigma-Aldrich). After addition of 10mM EGTA to stop the MNase action, nuclear pellet was resuspended in 1mL low-salt buffer (0.5X PBS, 5mM EGTA, 0.5mM PMSF, 1X complete protease inhibitor cocktail) complemented with 50 units of murine RNase inhibitor (#M0314S, NEB), and chromatin was extracted overnight at 4°C in an end-over-end rotator. After centrifugation, the supernatant was precleared with 30µL of protein A/G Plus agarose beads (#sc-2003,Santa Cruz Biotechnology, Dallas, TX) for 30 min at 4°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°C in an end-over-end rotator. CENP-A/primary antibody complex and mock-IP sample were immunoprecipitated with 50µL of protein A/G plus agarose beads for 2 hours at 4°C on the end-over-end rotator. Beads were washed three times with 1mL 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; 0.1M 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-401-4001, 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 mock-IP 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 +/- 2kb 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 171bp, the length of the α-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 α-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°C. The reaction was stopped by addition of 50mM EDTA (#351-027-721, Quality Biological, Gaithersburg, MD) and incubated at 75°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 α-satellite or cenRNA#4 primers (Supplemental Table 3). Cycling conditions for PCR were: 30s at 98°C; 30 cycles: 5s at 98°C, 30s at 57°C, 20s at 72°C; 300s at 72°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®570 or Quasar®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°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 1mg/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 (0.1µM 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°C in the dark. Finally, cells were washed twice with 10% deionized formamide in 2X SSC for 30 min at 37°C and once with 2X 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°C. After three washes in 1X PBS, cells were incubated with secondary antibody (goat anti-rabbit IgG (H+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 1mg/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

$1.2x10^6$ cells were mixed with 100µL of RT nucleofection reagent (#VACA-1001, Lonza, Allendale, NJ) and 7µL of plasmid containing shRNA, or a GFP control to quantify transfection efficiency (500ng/µL of Scrambled, cenRNA#4A, cenRNA#4B, α-satellite A, α-satellite B, H3-GFP). After electroporation with Nucleofector® Device (Lonza, Walkersville, MD) using program O-005 (for high viability), HeLa cells were resuspended in 500µl of warm media. 200µL 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 0.5µg/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 30s with cold 4% paraformaldehyde in PEM (80mM K-PIPES pH6.8; 5mM EGTA pH7; 0,2mM $MgCl_2$). After washing three times with cold PEM, soluble proteins were extracted for 5 min on ice with 0.5% Triton X-100 in CSK (10mM K-PIPES pH6.8, 100mM NaCl, 300mM sucrose, 1mM EGTA, 3mM $MgCl_2$). 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 1X TBS, 1% Bovine Serum Albumin, 5% normal goat serum overnight at 4°C in a humidified chamber. Cells were washed three times for 5 min at RT with 1X TBS, 0.1% Tween 20, and incubated with secondary antibody for 1 hour at RT. After washing, coverslips were mounted on slides with anti-fade 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 60X objective at 0.2 μm 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 N=3 biological replicates; typically, a minimum of 100 cells - 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, α 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 RIP-seq 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 α-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 α-satellite monomer (Supplemental Figure 1A), confirming the predominance of α-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 α-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 α-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 α-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 α-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 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 mitosis-early 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 newly-identified 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 α-satellite RNAs (Figure 2). Consensus centromeric transcripts were revealed by probes designed against the consensus sequence of α-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 ~28% and ~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 co-localization or partial co-localization of cenRNAs with CENP-B domains. Reassuringly, in cells expressing centromeric α-satellite transcripts, ~74% of them displayed overlap between CENP-B and α-satellite RNA signals (Figure 3B). The absence of RNA FISH signal after RNase A treatment

confirm that the observed α-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 α-satellite transcripts, cenRNA#4 was also found overlapping with CENP-B signal in ~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 α-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 (α-satellite), we observed discrete bands every ~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 α-satellite transcripts, several discrete bands were observed every ~170 bases after retro-transcription with either poly(dT) or random hexamer primers (Supplemental Figure 3B). However, when total RNAs were retro-transcribed, 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'-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 CENP-A/HJURP complexes.

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

In our earlier work, the down-regulation of consensus α-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 down-regulation 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 α-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 α-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 α-satellite transcripts (α-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 α-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 α-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 α-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 α-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 trans-migration 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 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 poly-adenylated 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-A/H4, thus acting as co-chaperone; third, cenRNAs may sequester or protect pre-assembly CENP-A/H4, preventing their fortuitious association with H3 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 CENP-As 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 (N=3).

Figure 3: cenRNAs and CENP-B domains partially co-localized. (A) Schematic of the co-IF/RNA FISH experiment. (B & C) G1-synchronized HeLa cells are stained for CENP-B, as marker of centromeres and centromeric transcripts (α-satellite in B and cenRNA#4 in C). Cells displaying an overlap of the IF and RNA signals were counted amongst cells expressing α-satellite transcripts and cenRNA#4. No signal was observed after RNase treatment (+RNase) (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 α-satellite or cenRNA#4 shRNA are synchronized at late mitosis – early G1 and stained for CENP-B (marker of centromeres) and α-tubulin (marker of mitotic spindle). Cells were counted and categorized for their chromosome defects (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 (~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 Rip-seq. 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 (N=3).

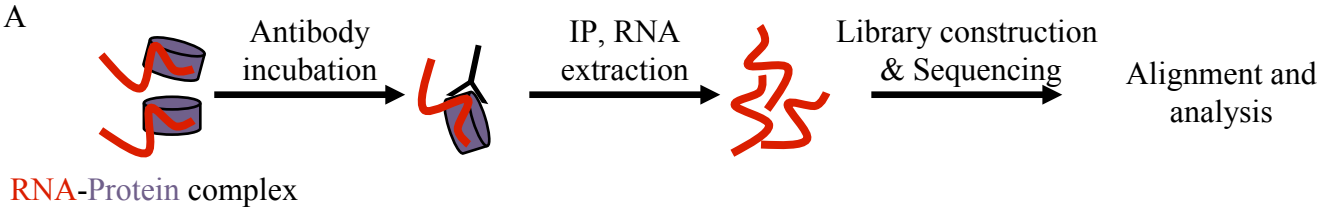
Supplemental Figure 3: RNAs transcribed from centromeres are poly-adenylated. (A) Using primers designed against centromeric α-satellite, total RNAs were amplified after retro-transcription with either poly-(dT) or random hexamer primers. (B) As in A, total RNAs were retro-transcribed and amplified with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

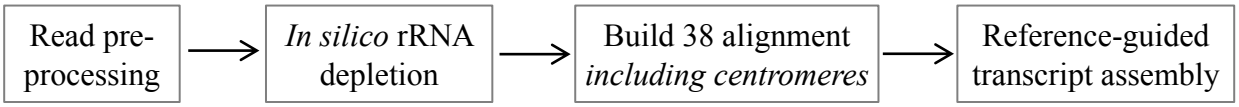
Supplemental figure 5: cenRNAs depletion leads to chromosome defects. (A) Schematic of the down-regulation of cenRNAs followed by co-IF experiment. (B) Transfected HeLa cells with either scrambled or α-satellite or cenRNA#4 shRNA are synchronized at late mitosis – early G1 and stained for CENP-B (marker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

Figure 1:

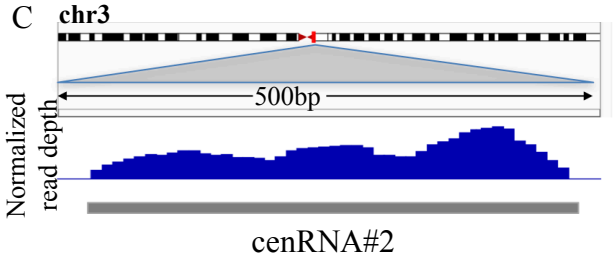
A



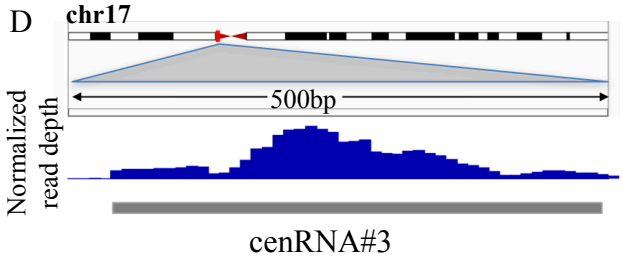
B



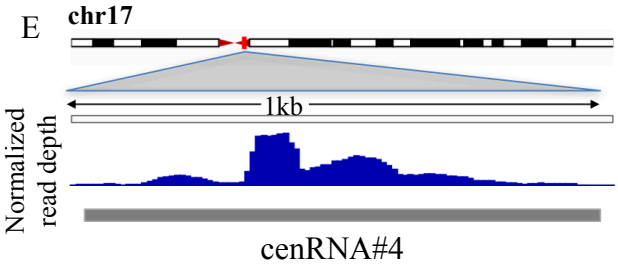
C



D



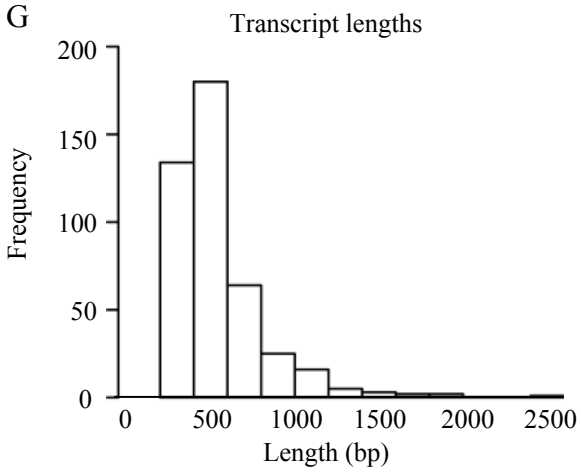
E



F

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

G



H

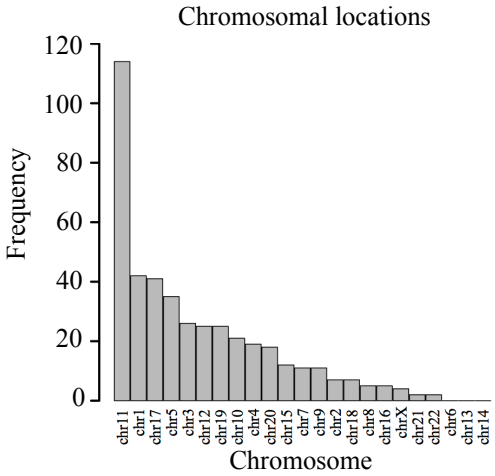
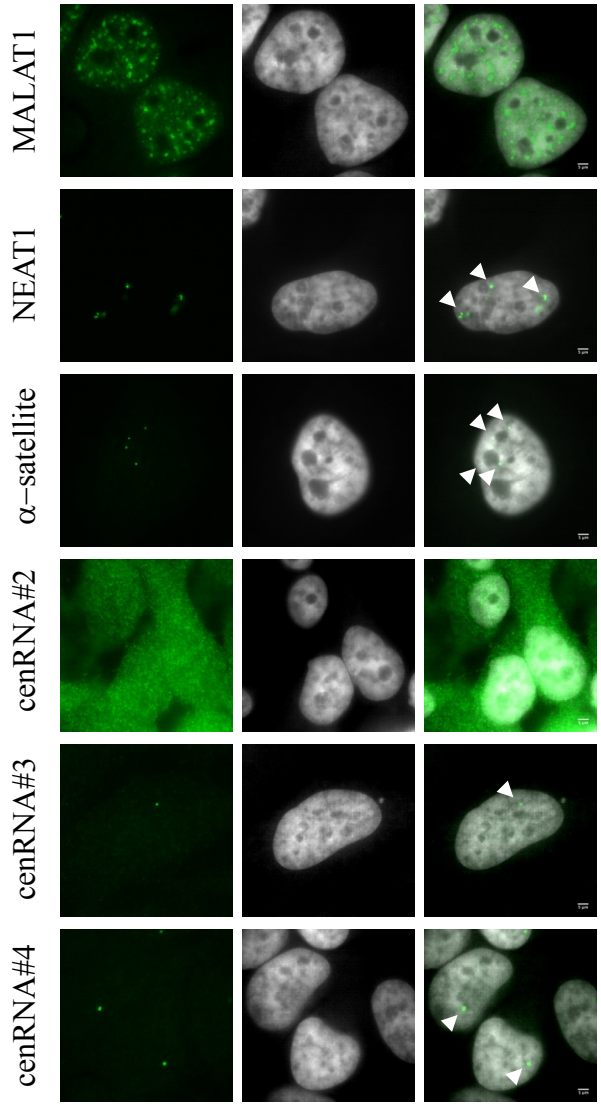


Figure 2:

A.

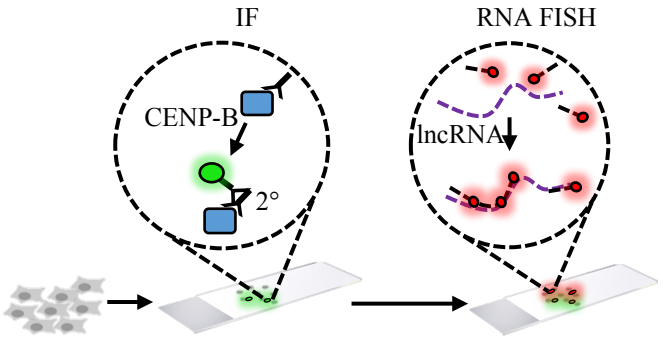


B.

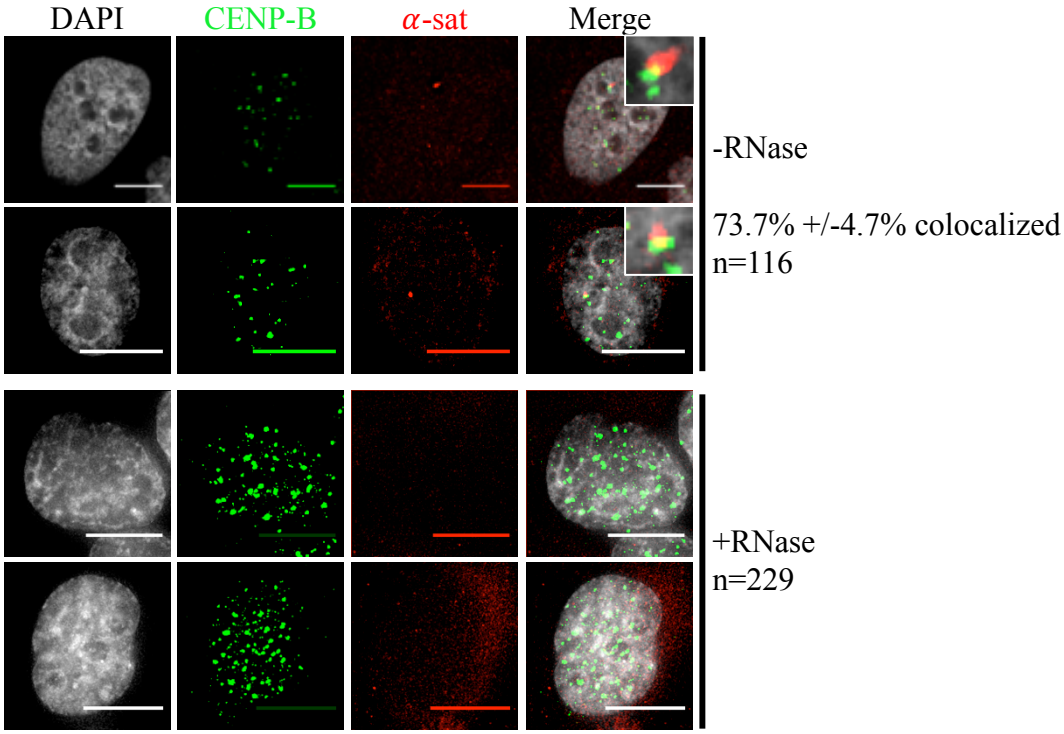
RNA	% of cells with an RNA signal	Standard deviation	Number of cells counted
NEAT	97.37	0.94	731
MALAT1	84.42	6.04	726
α-satellite	34.02	7.62	622
cenRNA#2	3.65	2.38	685
cenRNA#3	27.68	18.66	698
cenRNA#4	37.37	15.30	697

Figure 3:

A.


IF
RNA FISH
CENP-B
2°
lncRNA

B.


DAPI
CENP-B
α-sat
Merge
-RNase
73.7% +/-4.7% colocalized
n=116
+RNase
n=229

C.

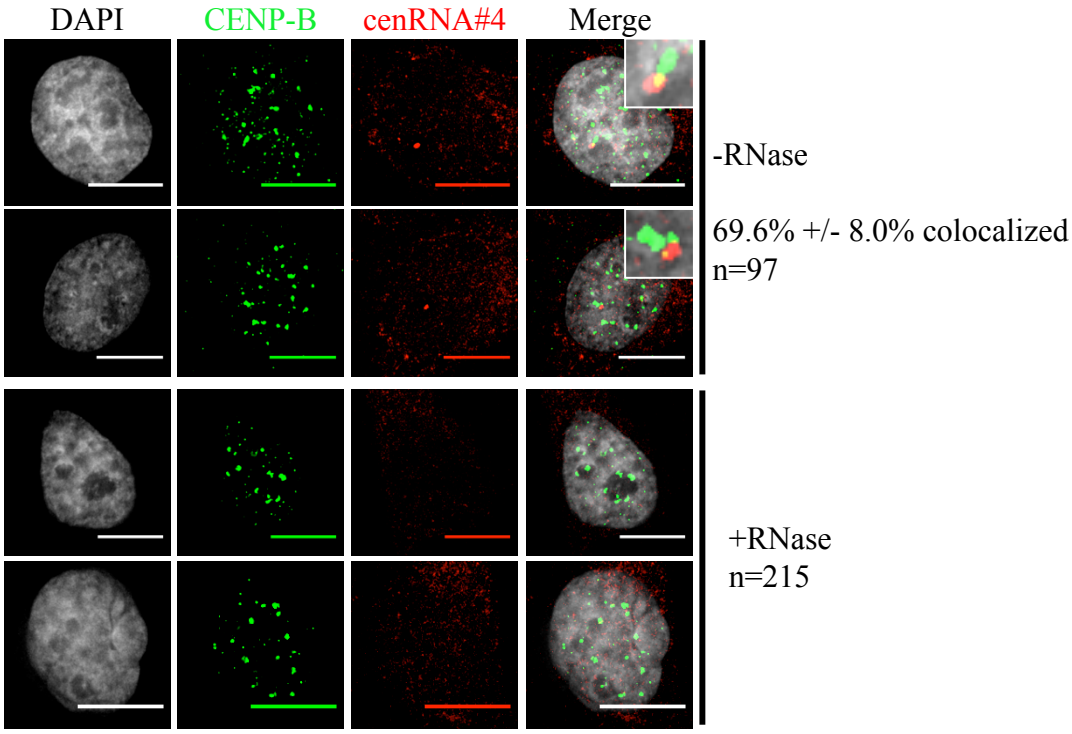
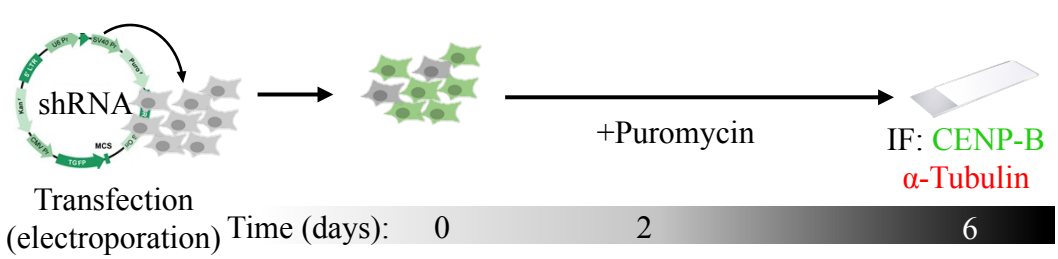

DAPI
CENP-B
cenRNA#4
Merge
-RNase
69.6% +/- 8.0% colocalized
n=97
+RNase
n=215

Figure 4:

A.


shRNA
Transfection
(electroporation)
Time (days):
0
2
6
+Puromycin
IF: CENP-B
α-Tubulin

B.

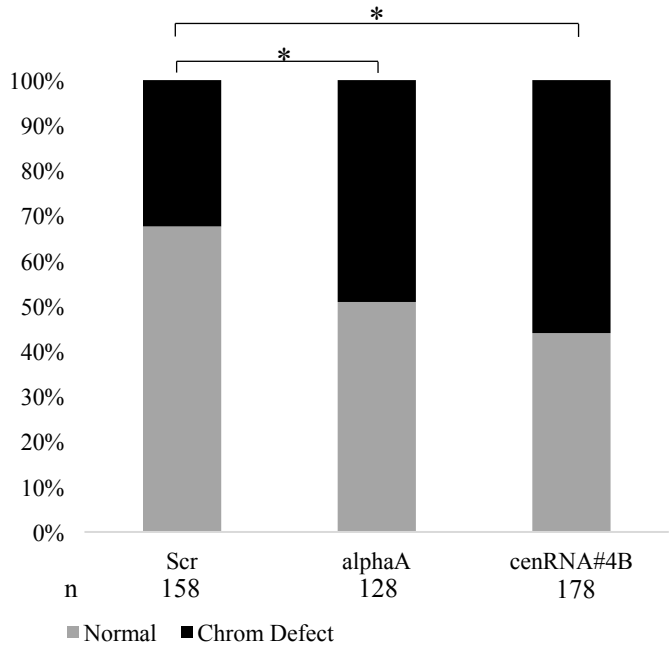
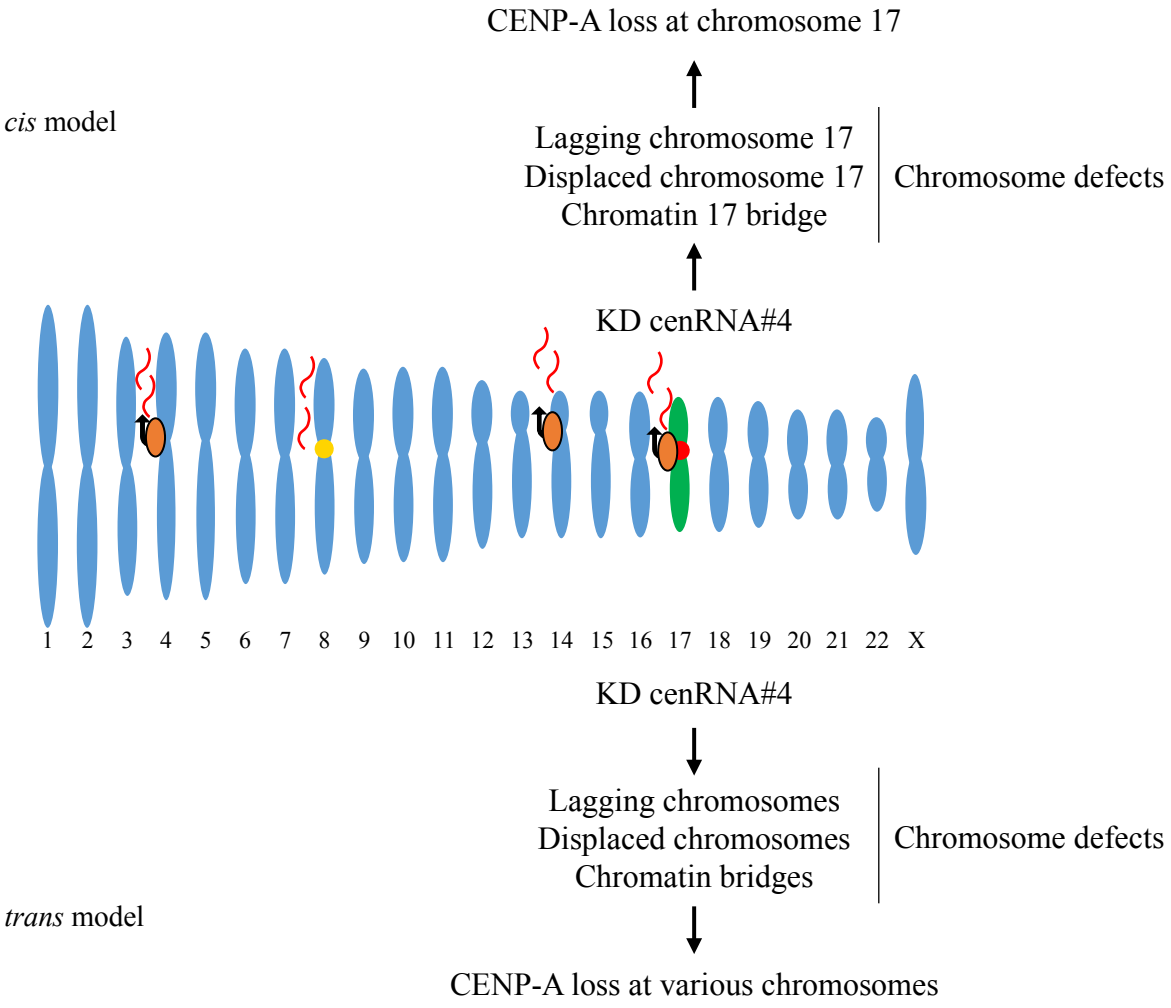
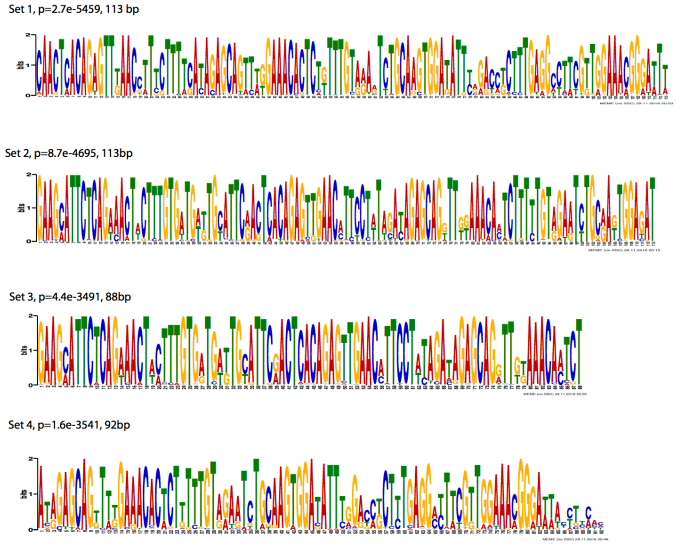

*
*
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Scr
alphaA
cenRNA#4B
n
158
128
178
Normal
Chrom Defect

Figure 5:

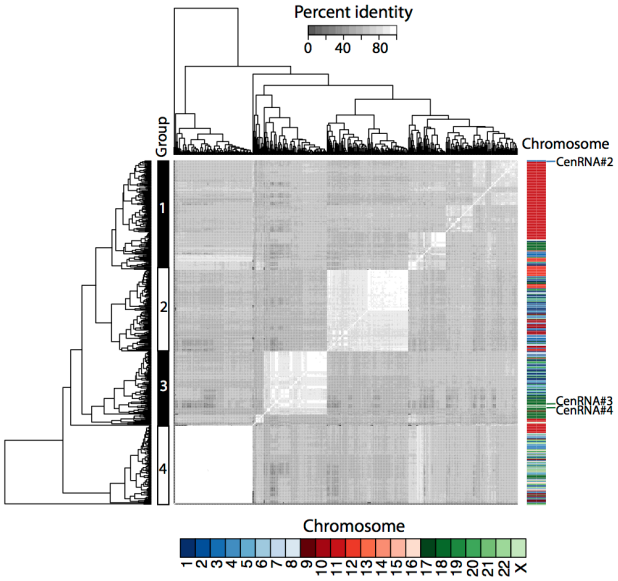

CENP-A loss at chromosome 17
cis model
Lagging chromosome 17
Displaced chromosome 17
Chromatin 17 bridge
Chromosome defects
KD cenRNA#4
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X
KD cenRNA#4
Lagging chromosomes
Displaced chromosomes
Chromatin bridges
Chromosome defects
trans model
CENP-A loss at various chromosomes

Supplemental Figure 1:

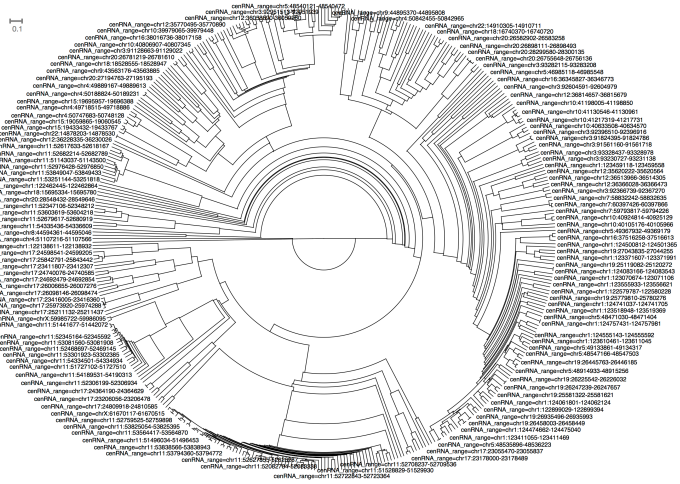
A.



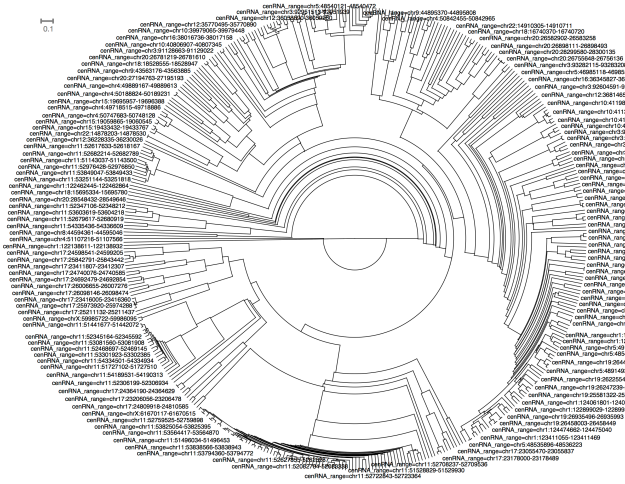
B.



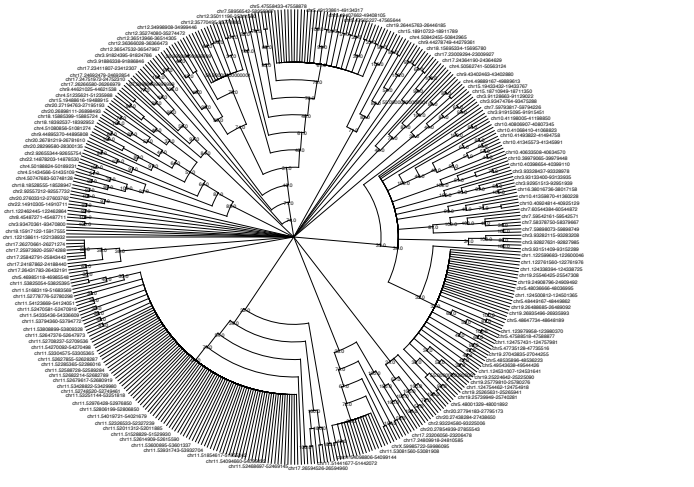
C.



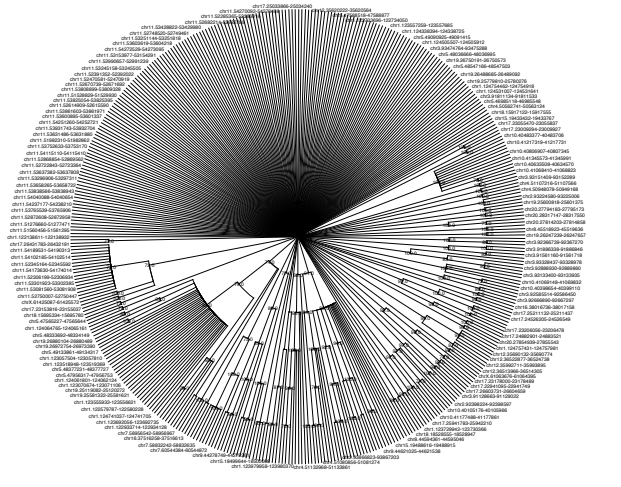
D.



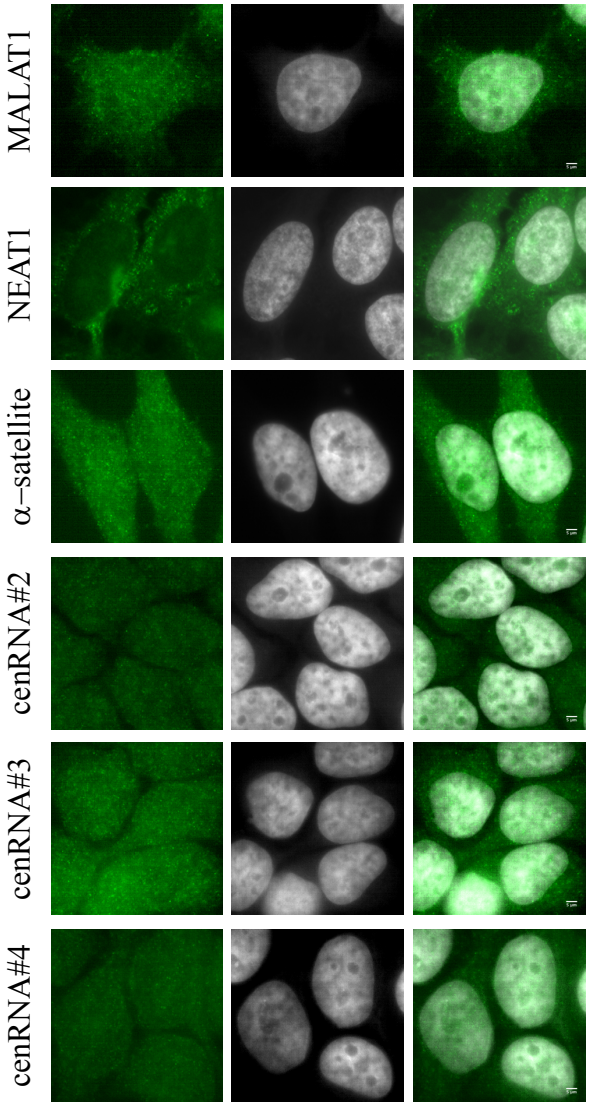
E.



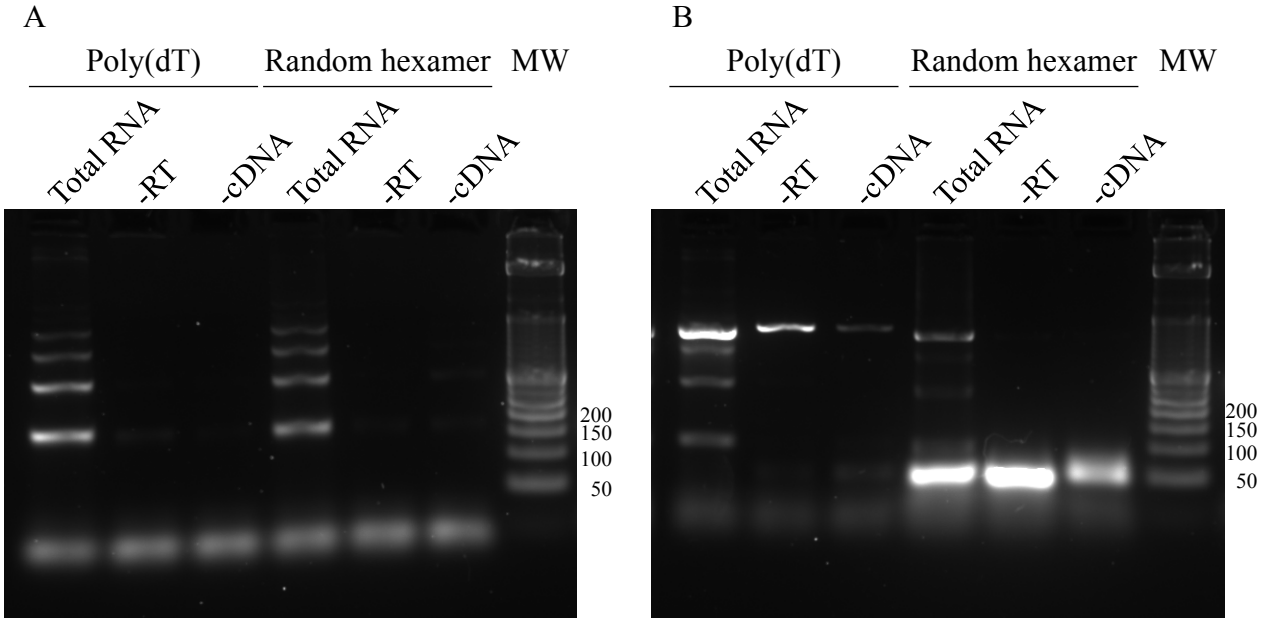
F.



Supplemental Figure 2



Supplemental Figure 3:

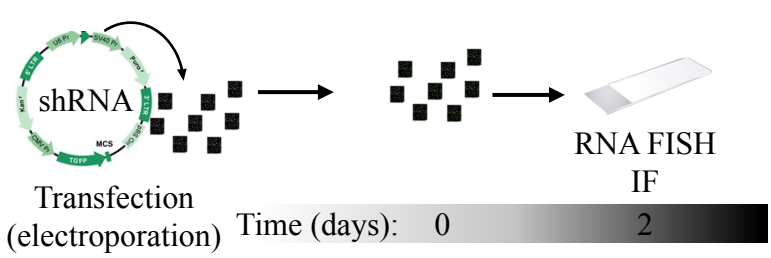


α-satellite primers

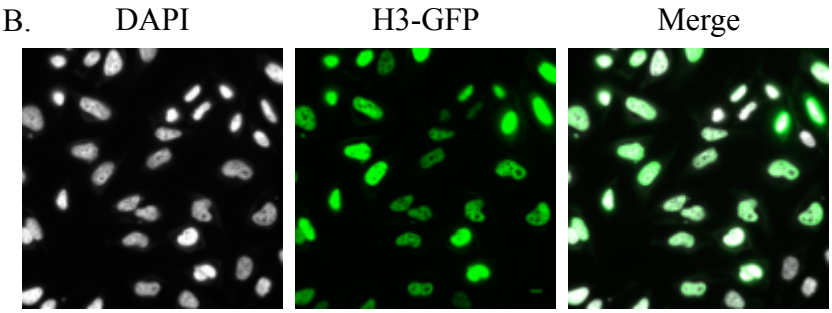
cenRNA#4 primers

Supplemental Figure 4:

A.

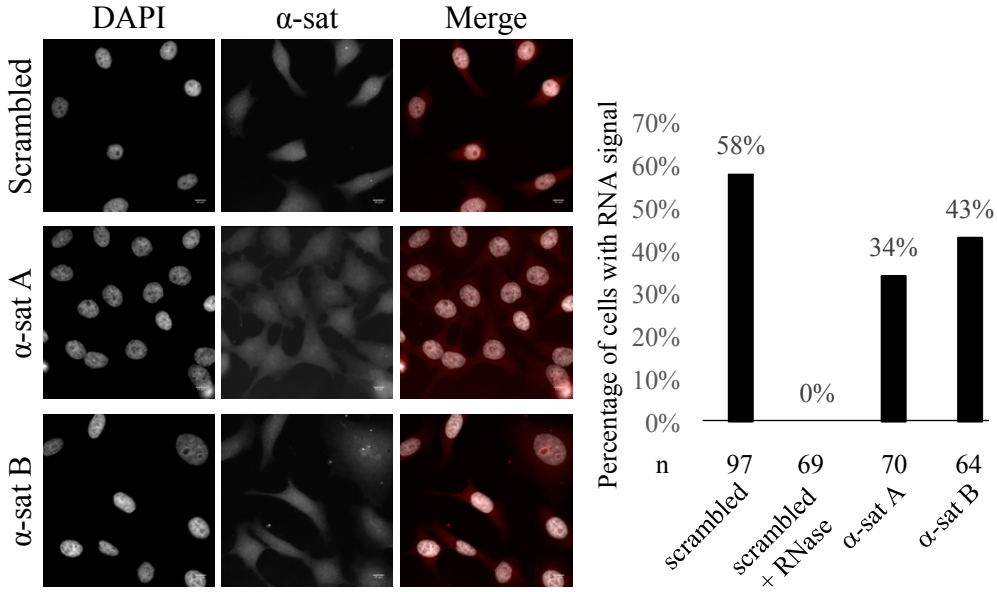


B.

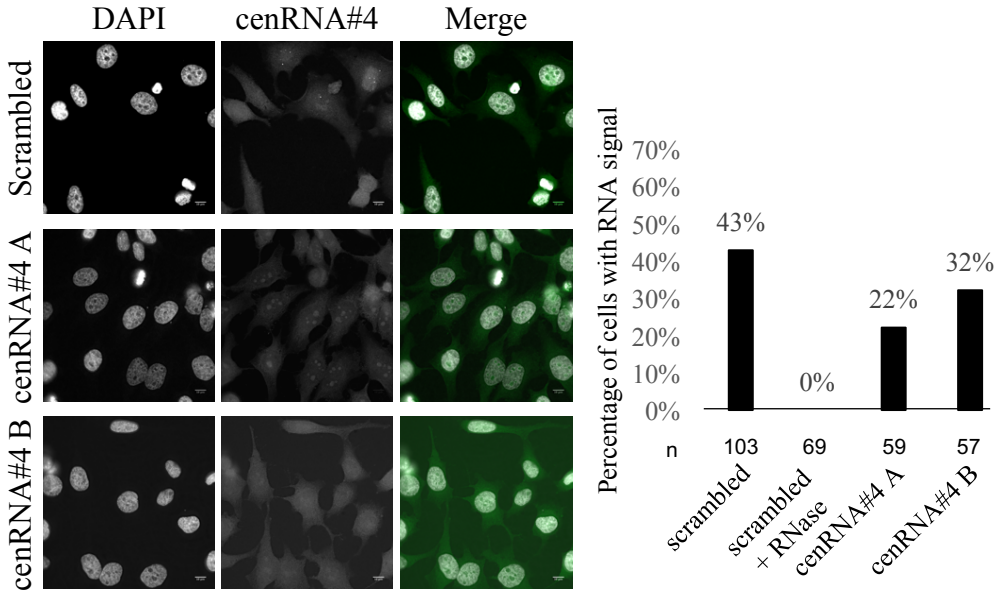


Transfection efficiency: 82.2% ± 3.1% (N=5)

C.

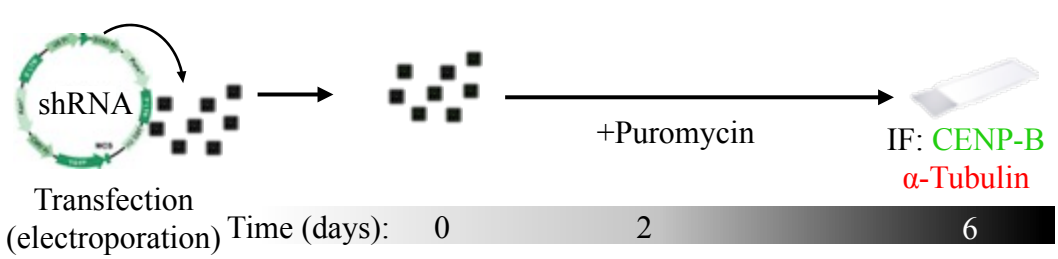


D.

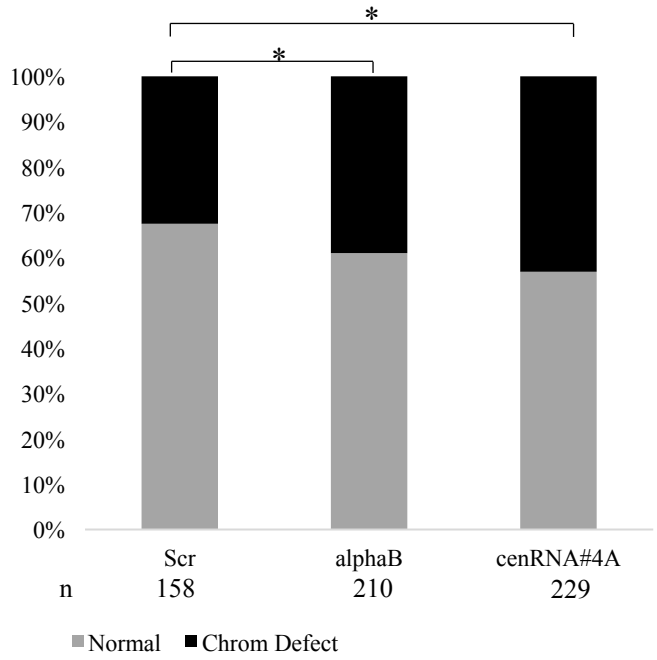


Supplemental Figure 5:

A.



B.



Supplemental Table 1: List of antibodies.

Target Protein	Reference	Manufacturer	Method
CENP-A “3-19”	ab13939	Abcam	RNA Immuno-Precipitation – sequencing, Immuno-Fluorescence
CENP-B “H65”	sc-22788	Santa Cruz	Immuno-Fluorescence
α-Tubulin “DM1A”	62204	Thermo Fisher Scientific	Immuno-Fluorescence

Supplemental Table 2: List of shRNA sequence.

Target Sequence	Sequence (5’ to 3’)
Scrambled	GCACTACCAGAGCTAACTCAGATAGTACT
α-satellite A	TGTGTGCATTCAACTCACAGAGTTG
α-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
α-satellite SetA	Forward	TGCATTCAACTCACAGAGTTGAAC	PCR
	Reverse	CATCACAAAGAAGTTTCTGAGAATGC	PCR
α-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	locus	chr	length
1	CenRNA2	chr3:93470360-93470800	chr3	440
2	CenRNA3	chr17:23016255-23016556	chr17	301
3	cenRNA:chr17:26594525-26594960	chr17:26594525-26594960	chr17	435
4	CenRNA4	chr17:26603730-26604659	chr17	929
5	cenRNA:chr17:24150840-24151314	chr17:24150840-24151314	chr17	474
6	cenRNA:chr19:25422901-25423243	chr19:25422901-25423243	chr19	342
7	cenRNA:chr12:35011195-35011560	chr12:35011195-35011560	chr12	365
8	cenRNA:chr5:47491561-47491892	chr5:47491561-47491892	chr5	331
9	cenRNA:chr19:25600817-25601375	chr19:25600817-25601375	chr19	558
10	cenRNA:chr17:24740075-24740585	chr17:24740075-24740585	chr17	510
11	cenRNA:chr19:26750190-26750573	chr19:26750190-26750573	chr19	383
12	cenRNA:chr20:27194762-27195193	chr20:27194762-27195193	chr20	431
13	cenRNA:chr5:48001328-48001892	chr5:48001328-48001892	chr5	564
14	cenRNA:chr17:26098145-26098474	chr17:26098145-26098474	chr17	329
15	cenRNA:chr5:48535895-48536223	chr5:48535895-48536223	chr5	328
16	cenRNA:chr10:40924813-40925129	chr10:40924813-40925129	chr10	316
17	cenRNA:chr12:36782697-36783180	chr12:36782697-36783180	chr12	483
18	cenRNA:chr4:50562740-50563124	chr4:50562740-50563124	chr4	384
19	cenRNA:chr20:28313055-28313356	chr20:28313055-28313356	chr20	301
20	cenRNA:chr11:51814030-51814362	chr11:51814030-51814362	chr11	332
21	cenRNA:chr18:16740369-16740720	chr18:16740369-16740720	chr18	351
22	cenRNA:chr17:25033865-25034240	chr17:25033865-25034240	chr17	375
23	cenRNA:chr12:36513965-36514305	chr12:36513965-36514305	chr12	340
24	cenRNA:chr1:123518947-123519369	chr1:123518947-123519369	chr1	422
25	cenRNA:chr17:24187861-24188440	chr17:24187861-24188440	chr17	579
26	cenRNA:chr12:35427176-35427564	chr12:35427176-35427564	chr12	388
27	cenRNA:chr19:27146703-27147147	chr19:27146703-27147147	chr19	444
28	cenRNA:chr15:18780386-18781210	chr15:18780386-18781210	chr15	824
29	cenRNA:chr10:41013772-41014155	chr10:41013772-41014155	chr10	383
30	cenRNA:chr10:41068409-41068823	chr10:41068409-41068823	chr10	414
31	cenRNA:chr2:92598948-92599257	chr2:92598948-92599257	chr2	309
32	cenRNA:chr4:51107215-51107566	chr4:51107215-51107566	chr4	351
33	cenRNA:chr11:53631485-53631880	chr11:53631485-53631880	chr11	395
34	cenRNA:chr18:15885398-15885724	chr18:15885398-15885724	chr18	326
35	cenRNA:chr22:14878202-14878530	chr22:14878202-14878530	chr22	328
36	cenRNA:chr2:93866822-93867203	chr2:93866822-93867203	chr2	381
37	cenRNA:chr10:39979064-39979448	chr10:39979064-39979448	chr10	384
38	cenRNA:chr19:26880103-26880489	chr19:26880103-26880489	chr19	386
39	cenRNA:chr11:54102184-54102514	chr11:54102184-54102514	chr11	330
40	cenRNA:chr2:92655343-92655754	chr2:92655343-92655754	chr2	411
41	cenRNA:chr1:123128673-123129060	chr1:123128673-123129060	chr1	387

42	cenRNA:chr1:123070673-123071106	chr1:123070673-123071106	chr1	433
43	cenRNA:chr12:35774447-35774979	chr12:35774447-35774979	chr12	532
44	cenRNA:chr4:51124734-51125721	chr4:51124734-51125721	chr4	987
45	cenRNA:chr5:47310450-47310774	chr5:47310450-47310774	chr5	324
46	cenRNA:chr17:25211131-25211437	chr17:25211131-25211437	chr17	306
47	cenRNA:chr1:123729941-123730366	chr1:123729941-123730366	chr1	425
48	cenRNA:chr17:26572643-26573713	chr17:26572643-26573713	chr17	1070
49	cenRNA:chr17:24751971-24752310	chr17:24751971-24752310	chr17	339
50	cenRNA:chr1:123550662-123550969	chr1:123550662-123550969	chr1	307
51	cenRNA:chr2:92398223-92398597	chr2:92398223-92398597	chr2	374
52	cenRNA:chr12:35620221-35620564	chr12:35620221-35620564	chr12	343
53	cenRNA:chr3:92699663-92700018	chr3:92699663-92700018	chr3	355
54	cenRNA:chr1:124757430-124757981	chr1:124757430-124757981	chr1	551
55	cenRNA:chr8:45463531-45463856	chr8:45463531-45463856	chr8	325
56	cenRNA:chr11:52722842-52723364	chr11:52722842-52723364	chr11	522
57	cenRNA:chr11:54270091-54270498	chr11:54270091-54270498	chr11	407
58	cenRNA:chr10:41177487-41177861	chr10:41177487-41177861	chr10	374
59	cenRNA:chr11:52882791-52883243	chr11:52882791-52883243	chr11	452
60	cenRNA:chr1:124083165-124083543	chr1:124083165-124083543	chr1	378
61	cenRNA:chr11:53682092-53682929	chr11:53682092-53682929	chr11	837
62	cenRNA:chr15:18910721-18911789	chr15:18910721-18911789	chr15	1068
63	cenRNA:chr1:123411054-123411469	chr1:123411054-123411469	chr1	415
64	cenRNA:chr17:25973919-25974288	chr17:25973919-25974288	chr17	369
65	cenRNA:chr20:26755647-26756136	chr20:26755647-26756136	chr20	489
66	cenRNA:chr11:53245157-53245505	chr11:53245157-53245505	chr11	348
67	cenRNA:chr5:48914932-48915256	chr5:48914932-48915256	chr5	324
68	cenRNA:chr15:18499643-18500068	chr15:18499643-18500068	chr15	425
69	cenRNA:chr1:124474661-124475040	chr1:124474661-124475040	chr1	379
70	cenRNA:chr1:122733695-122734050	chr1:122733695-122734050	chr1	355
71	cenRNA:chr11:53244246-53244701	chr11:53244246-53244701	chr11	455
72	cenRNA:chr7:58832241-58832635	chr7:58832241-58832635	chr7	394
73	cenRNA:chr7:60699852-60700209	chr7:60699852-60700209	chr7	357
74	cenRNA:chr12:36058889-36059260	chr12:36058889-36059260	chr12	371
75	cenRNA:chr15:18586782-18587204	chr15:18586782-18587204	chr15	422
76	cenRNA:chr1:123527773-123528211	chr1:123527773-123528211	chr1	438
77	cenRNA:chr11:53081559-53081908	chr11:53081559-53081908	chr11	349
78	cenRNA:chr15:18710948-18711350	chr15:18710948-18711350	chr15	402
79	cenRNA:chr11:52858028-52858472	chr11:52858028-52858472	chr11	444
80	cenRNA:chr19:27043834-27044255	chr19:27043834-27044255	chr19	421
81	cenRNA:chr19:26488684-26489092	chr19:26488684-26489092	chr19	408
82	cenRNA:chr20:27673257-27673868	chr20:27673257-27673868	chr20	611
83	cenRNA:chr11:51854616-51855242	chr11:51854616-51855242	chr11	626

84	cenRNA:chr17:23416004-23416360	chr17:23416004-23416360	chr17	356
85	cenRNA:chr1:124741036-124741705	chr1:124741036-124741705	chr1	669
86	cenRNA:chr3:91915094-91915451	chr3:91915094-91915451	chr3	357
87	cenRNA:chr8:45518922-45519636	chr8:45518922-45519636	chr8	714
88	cenRNA:chr8:45487270-45487711	chr8:45487270-45487711	chr8	441
89	cenRNA:chr10:41359869-41360228	chr10:41359869-41360228	chr10	359
90	cenRNA:chr3:91128662-91129022	chr3:91128662-91129022	chr3	360
91	cenRNA:chr9:43402462-43402880	chr9:43402462-43402880	chr9	418
92	cenRNA:chr1:123692055-123692735	chr1:123692055-123692735	chr1	680
93	cenRNA:chr11:52976427-52976850	chr11:52976427-52976850	chr11	423
94	cenRNA:chr10:40398653-40399110	chr10:40398653-40399110	chr10	457
95	cenRNA:chr1:124061800-124062124	chr1:124061800-124062124	chr1	324
96	cenRNA:chr11:53808898-53809328	chr11:53808898-53809328	chr11	430
97	cenRNA:chr5:49090924-49091415	chr5:49090924-49091415	chr5	491
98	cenRNA:chr11:53301922-53302385	chr11:53301922-53302385	chr11	463
99	cenRNA:chr10:40633507-40634570	chr10:40633507-40634570	chr10	1063
100	cenRNA:chrX:59985721-59986095	chrX:59985721-59986095	chrX	374
101	cenRNA:chr19:25265630-25265941	chr19:25265630-25265941	chr19	311
102	cenRNA:chr19:26445762-26446185	chr19:26445762-26446185	chr19	423
103	cenRNA:chr10:40483376-40483706	chr10:40483376-40483706	chr10	330
104	cenRNA:chr11:51727101-51727510	chr11:51727101-51727510	chr11	409
105	cenRNA:chr11:53752632-53753170	chr11:53752632-53753170	chr11	538
106	cenRNA:chr16:37232571-37232936	chr16:37232571-37232936	chr16	365
107	cenRNA:chr19:25739948-25740281	chr19:25739948-25740281	chr19	333
108	cenRNA:chr5:48250476-48250874	chr5:48250476-48250874	chr5	398
109	cenRNA:chr10:41069147-41069832	chr10:41069147-41069832	chr10	685
110	cenRNA:chr3:91561159-91561718	chr3:91561159-91561718	chr3	559
111	cenRNA:chr15:19695956-19696388	chr15:19695956-19696388	chr15	432
112	cenRNA:chr18:18392536-18392952	chr18:18392536-18392952	chr18	416
113	cenRNA:chr11:54115109-54115410	chr11:54115109-54115410	chr11	301
114	cenRNA:chr17:23411806-23412307	chr17:23411806-23412307	chr17	501
115	cenRNA:chr11:52617632-52618167	chr11:52617632-52618167	chr11	535
116	cenRNA:chr5:47956316-47956753	chr5:47956316-47956753	chr5	437
117	cenRNA:chr10:41295831-41296219	chr10:41295831-41296219	chr10	388
118	cenRNA:chr10:40127909-40129567	chr10:40127909-40129567	chr10	1658
119	cenRNA:chr8:45530197-45530952	chr8:45530197-45530952	chr8	755
120	cenRNA:chr11:54059889-54060246	chr11:54059889-54060246	chr11	357
121	cenRNA:chr19:26225541-26226032	chr19:26225541-26226032	chr19	491
122	cenRNA:chr1:122579786-122580228	chr1:122579786-122580228	chr1	442
123	cenRNA:chr11:53266324-53266800	chr11:53266324-53266800	chr11	476
124	cenRNA:chr17:26431782-26432191	chr17:26431782-26432191	chr17	409
125	cenRNA:chr12:35274079-35274472	chr12:35274079-35274472	chr12	393

126	cenRNA:chr1:124052682-124053024	chr1:124052682-124053024	chr1	342
127	cenRNA:chr17:25941782-25942210	chr17:25941782-25942210	chr17	428
128	cenRNA:chr5:47588517-47588877	chr5:47588517-47588877	chr5	360
129	cenRNA:chr5:47558432-47558878	chr5:47558432-47558878	chr5	446
130	cenRNA:chr11:51092592-51093123	chr11:51092592-51093123	chr11	531
131	cenRNA:chr19:25224641-25225090	chr19:25224641-25225090	chr19	449
132	cenRNA:chr11:53375117-53375704	chr11:53375117-53375704	chr11	587
133	cenRNA:chr5:49367931-49369179	chr5:49367931-49369179	chr5	1248
134	cenRNA:chr17:26548702-26549136	chr17:26548702-26549136	chr17	434
135	cenRNA:chr5:48893293-48893658	chr5:48893293-48893658	chr5	365
136	cenRNA:chr4:51080855-51081274	chr4:51080855-51081274	chr4	419
137	cenRNA:chr11:53916809-53917157	chr11:53916809-53917157	chr11	348
138	cenRNA:chr12:37081816-37082218	chr12:37081816-37082218	chr12	402
139	cenRNA:chr4:51434565-51435109	chr4:51434565-51435109	chr4	544
140	cenRNA:chr10:40806906-40807345	chr10:40806906-40807345	chr10	439
141	cenRNA:chr17:23055469-23055837	chr17:23055469-23055837	chr17	368
142	cenRNA:chr17:24364189-24364629	chr17:24364189-24364629	chr17	440
143	cenRNA:chr5:48540120-48540472	chr5:48540120-48540472	chr5	352
144	cenRNA:chr19:24934236-24934645	chr19:24934236-24934645	chr19	409
145	cenRNA:chr5:47797583-47797937	chr5:47797583-47797937	chr5	354
146	cenRNA:chr19:27162721-27163465	chr19:27162721-27163465	chr19	744
147	cenRNA:chr5:46985117-46985548	chr5:46985117-46985548	chr5	431
148	cenRNA:chr10:41176757-41177282	chr10:41176757-41177282	chr10	525
149	cenRNA:chr11:53980600-53981014	chr11:53980600-53981014	chr11	414
150	cenRNA:chr7:60544383-60544872	chr7:60544383-60544872	chr7	489
151	cenRNA:chr5:48547165-48547503	chr5:48547165-48547503	chr5	338
152	cenRNA:chr10:40105175-40105966	chr10:40105175-40105966	chr10	791
153	cenRNA:chr11:54040087-54040654	chr11:54040087-54040654	chr11	567
154	cenRNA:chr11:53564416-53564870	chr11:53564416-53564870	chr11	454
155	cenRNA:chr12:35619403-35619762	chr12:35619403-35619762	chr12	359
156	cenRNA:chr21:12739650-12740106	chr21:12739650-12740106	chr21	456
157	cenRNA:chr9:44621024-44621538	chr9:44621024-44621538	chr9	514
158	cenRNA:chr11:51982309-51982862	chr11:51982309-51982862	chr11	553
159	cenRNA:chr5:50036126-50036487	chr5:50036126-50036487	chr5	361
160	cenRNA:chr5:49543637-49544426	chr5:49543637-49544426	chr5	789
161	cenRNA:chr1:122599682-122600046	chr1:122599682-122600046	chr1	364
162	cenRNA:chr9:43800776-43801222	chr9:43800776-43801222	chr9	446
163	cenRNA:chrX:61425086-61425572	chrX:61425086-61425572	chrX	486
164	cenRNA:chr3:92951512-92951939	chr3:92951512-92951939	chr3	427
165	cenRNA:chr16:38019280-38019628	chr16:38019280-38019628	chr16	348
166	cenRNA:chr1:122510753-122511060	chr1:122510753-122511060	chr1	307
167	cenRNA:chr12:36547531-36547967	chr12:36547531-36547967	chr12	436

168	cenRNA:chr11:52759524-52759898	chr11:52759524-52759898	chr11	374
169	cenRNA:chr10:41130545-41130961	chr10:41130545-41130961	chr10	416
170	cenRNA:chr5:48333691-48334149	chr5:48333691-48334149	chr5	458
171	cenRNA:chr12:35770494-35770890	chr12:35770494-35770890	chr12	396
172	cenRNA:chr9:44895369-44895808	chr9:44895369-44895808	chr9	439
173	cenRNA:chr3:92358403-92358821	chr3:92358403-92358821	chr3	418
174	cenRNA:chr10:41345572-41345991	chr10:41345572-41345991	chr10	419
175	cenRNA:chr12:35965549-35967067	chr12:35965549-35967067	chr12	1518
176	cenRNA:chr7:60397425-60397866	chr7:60397425-60397866	chr7	441
177	cenRNA:chr1:122462444-122462864	chr1:122462444-122462864	chr1	420
178	cenRNA:chr16:37516257-37516613	chr16:37516257-37516613	chr16	356
179	cenRNA:chr11:53838565-53838943	chr11:53838565-53838943	chr11	378
180	cenRNA:chr17:23009293-23009927	chr17:23009293-23009927	chr17	634
181	cenRNA:chr11:53600894-53601337	chr11:53600894-53601337	chr11	443
182	cenRNA:chr20:26582901-26583258	chr20:26582901-26583258	chr20	357
183	cenRNA:chr20:28548431-28549646	chr20:28548431-28549646	chr20	1215
184	cenRNA:chr11:52679616-52680919	chr11:52679616-52680919	chr11	1303
185	cenRNA:chr1:124253782-124254140	chr1:124253782-124254140	chr1	358
186	cenRNA:chr4:49889166-49889613	chr4:49889166-49889613	chr4	447
187	cenRNA:chr3:93133399-93133935	chr3:93133399-93133935	chr3	536
188	cenRNA:chr2:93224579-93225006	chr2:93224579-93225006	chr2	427
189	cenRNA:chr11:53153976-53154291	chr11:53153976-53154291	chr11	315
190	cenRNA:chr11:52697347-52697708	chr11:52697347-52697708	chr11	361
191	cenRNA:chr11:52795266-52796417	chr11:52795266-52796417	chr11	1151
192	cenRNA:chr5:48205766-48206194	chr5:48205766-48206194	chr5	428
193	cenRNA:chr1:124505506-124505912	chr1:124505506-124505912	chr1	406
194	cenRNA:chr11:52470580-52470919	chr11:52470580-52470919	chr11	339
195	cenRNA:chr20:27603311-27603762	chr20:27603311-27603762	chr20	451
196	cenRNA:chr5:48183312-48183764	chr5:48183312-48183764	chr5	452
197	cenRNA:chr11:52049738-52050078	chr11:52049738-52050078	chr11	340
198	cenRNA:chr5:48245126-48245649	chr5:48245126-48245649	chr5	523
199	cenRNA:chr21:12552940-12553283	chr21:12552940-12553283	chr21	343
200	cenRNA:chr17:24598540-24599205	chr17:24598540-24599205	chr17	665
201	cenRNA:chr11:52447518-52447886	chr11:52447518-52447886	chr11	368
202	cenRNA:chr11:53765538-53765906	chr11:53765538-53765906	chr11	368
203	cenRNA:chr11:53554142-53554649	chr11:53554142-53554649	chr11	507
204	cenRNA:chr20:26781218-26781610	chr20:26781218-26781610	chr20	392
205	cenRNA:chr3:91824394-91824786	chr3:91824394-91824786	chr3	392
206	cenRNA:chr4:49858740-49859432	chr4:49858740-49859432	chr4	692
207	cenRNA:chr17:25442364-25442921	chr17:25442364-25442921	chr17	557
208	cenRNA:chr3:92618206-92618577	chr3:92618206-92618577	chr3	371
209	cenRNA:chr11:54019720-54021679	chr11:54019720-54021679	chr11	1959

210	cenRNA:chr17:22815930-22816652	chr17:22815930-22816652	chr17	722
211	cenRNA:chr18:15695333-15695780	chr18:15695333-15695780	chr18	447
212	cenRNA:chr11:52872607-52872958	chr11:52872607-52872958	chr11	351
213	cenRNA:chr15:19488615-19488915	chr15:19488615-19488915	chr15	300
214	cenRNA:chr12:36465198-36465550	chr12:36465198-36465550	chr12	352
215	cenRNA:chr11:54251259-54252721	chr11:54251259-54252721	chr11	1462
216	cenRNA:chr11:51683118-51683569	chr11:51683118-51683569	chr11	451
217	cenRNA:chr11:52682213-52682789	chr11:52682213-52682789	chr11	576
218	cenRNA:chr10:41198004-41198850	chr10:41198004-41198850	chr10	846
219	cenRNA:chr11:51966780-51967479	chr11:51966780-51967479	chr11	699
220	cenRNA:chr5:48036665-48036995	chr5:48036665-48036995	chr5	330
221	cenRNA:chr20:27814202-27814858	chr20:27814202-27814858	chr20	656
222	cenRNA:chr5:49133860-49134317	chr5:49133860-49134317	chr5	457
223	cenRNA:chr20:26898110-26898493	chr20:26898110-26898493	chr20	383
224	cenRNA:chr1:124338393-124338725	chr1:124338393-124338725	chr1	332
225	cenRNA:chr9:43563175-43563885	chr9:43563175-43563885	chr9	710
226	cenRNA:chr1:124531006-124531641	chr1:124531006-124531641	chr1	635
227	cenRNA:chr3:92585513-92586450	chr3:92585513-92586450	chr3	937
228	cenRNA:chr11:52708236-52709536	chr11:52708236-52709536	chr11	1300
229	cenRNA:chr1:123057503-123057810	chr1:123057503-123057810	chr1	307
230	cenRNA:chr11:53849046-53849433	chr11:53849046-53849433	chr11	387
231	cenRNA:chr10:41217318-41217731	chr10:41217318-41217731	chr10	413
232	cenRNA:chr11:51289660-51290100	chr11:51289660-51290100	chr11	440
233	cenRNA:chr5:47735127-47735516	chr5:47735127-47735516	chr5	389
234	cenRNA:chr17:26006654-26007276	chr17:26006654-26007276	chr17	622
235	cenRNA:chr1:123459117-123459558	chr1:123459117-123459558	chr1	441
236	cenRNA:chr12:36488356-36488693	chr12:36488356-36488693	chr12	337
237	cenRNA:chr11:52011311-52011885	chr11:52011311-52011885	chr11	574
238	cenRNA:chr17:23973175-23973856	chr17:23973175-23973856	chr17	681
239	cenRNA:chr17:22941094-22941749	chr17:22941094-22941749	chr17	655
240	cenRNA:chr20:27854938-27855543	chr20:27854938-27855543	chr20	605
241	cenRNA:chr1:122725297-122725665	chr1:122725297-122725665	chr1	368
242	cenRNA:chr19:26972753-26973390	chr19:26972753-26973390	chr19	637
243	cenRNA:chr11:54335435-54336609	chr11:54335435-54336609	chr11	1174
244	cenRNA:chr11:52588727-52589284	chr11:52588727-52589284	chr11	557
245	cenRNA:chr12:36228334-36230026	chr12:36228334-36230026	chr12	1692
246	cenRNA:chr9:45412381-45412834	chr9:45412381-45412834	chr9	453
247	cenRNA:chr7:58956541-58956967	chr7:58956541-58956967	chr7	426
248	cenRNA:chr3:91886337-91886846	chr3:91886337-91886846	chr3	509
249	cenRNA:chr3:91811133-91811533	chr3:91811133-91811533	chr3	400
250	cenRNA:chr4:50842454-50842965	chr4:50842454-50842965	chr4	511
251	cenRNA:chr17:24526204-24526549	chr17:24526204-24526549	chr17	345

252	cenRNA:chr19:26602103-26602448	chr19:26602103-26602448	chr19	345
253	cenRNA:chr11:54272528-54273095	chr11:54272528-54273095	chr11	567
254	cenRNA:chr11:53658264-53658722	chr11:53658264-53658722	chr11	458
255	cenRNA:chr11:52306198-52306934	chr11:52306198-52306934	chr11	736
256	cenRNA:chr9:43423820-43424501	chr9:43423820-43424501	chr9	681
257	cenRNA:chr3:93328436-93328978	chr3:93328436-93328978	chr3	542
258	cenRNA:chr11:52465481-52466218	chr11:52465481-52466218	chr11	737
259	cenRNA:chr19:25119081-25120272	chr19:25119081-25120272	chr19	1191
260	cenRNA:chr12:36814656-36815679	chr12:36814656-36815679	chr12	1023
261	cenRNA:chr5:47926212-47926617	chr5:47926212-47926617	chr5	405
262	cenRNA:chr1:123555932-123556621	chr1:123555932-123556621	chr1	689
263	cenRNA:chr19:25072669-25073018	chr19:25072669-25073018	chr19	349
264	cenRNA:chr3:92396509-92396916	chr3:92396509-92396916	chr3	407
265	cenRNA:chr3:92666889-92667297	chr3:92666889-92667297	chr3	408
266	cenRNA:chr4:50188823-50189231	chr4:50188823-50189231	chr4	408
267	cenRNA:chr4:51132967-51133861	chr4:51132967-51133861	chr4	894
268	cenRNA:chr17:26326121-26326787	chr17:26326121-26326787	chr17	666
269	cenRNA:chr11:51560455-51561295	chr11:51560455-51561295	chr11	840
270	cenRNA:chr19:25779809-25780276	chr19:25779809-25780276	chr19	467
271	cenRNA:chr4:50707213-50707594	chr4:50707213-50707594	chr4	381
272	cenRNA:chr5:48377230-48377727	chr5:48377230-48377727	chr5	497
273	cenRNA:chr9:44499269-44499824	chr9:44499269-44499824	chr9	555
274	cenRNA:chr7:59542160-59542571	chr7:59542160-59542571	chr7	411
275	cenRNA:chr19:26935495-26935993	chr19:26935495-26935993	chr19	498
276	cenRNA:chr1:122138610-122138932	chr1:122138610-122138932	chr1	322
277	cenRNA:chr11:52750006-52750447	chr11:52750006-52750447	chr11	441
278	cenRNA:chr1:123979957-123980370	chr1:123979957-123980370	chr1	413
279	cenRNA:chr11:53794359-53794772	chr11:53794359-53794772	chr11	413
280	cenRNA:chr12:36854676-36855089	chr12:36854676-36855089	chr12	413
281	cenRNA:chr18:19555252-19555606	chr18:19555252-19555606	chr18	354
282	cenRNA:chr11:51641632-51642075	chr11:51641632-51642075	chr11	443
283	cenRNA:chr5:48622293-48622971	chr5:48622293-48622971	chr5	678
284	cenRNA:chr19:25546424-25547308	chr19:25546424-25547308	chr19	884
285	cenRNA:chr3:92827630-92827985	chr3:92827630-92827985	chr3	355
286	cenRNA:chr11:52285364-52286016	chr11:52285364-52286016	chr11	652
287	cenRNA:chr11:53116440-53117183	chr11:53116440-53117183	chr11	743
288	cenRNA:chr4:50747682-50748128	chr4:50747682-50748128	chr4	446
289	cenRNA:chr9:44251165-44251701	chr9:44251165-44251701	chr9	536
290	cenRNA:chr1:122761559-122761976	chr1:122761559-122761976	chr1	417
291	cenRNA:chr4:51719445-51720071	chr4:51719445-51720071	chr4	626
292	cenRNA:chr11:52468696-52469145	chr11:52468696-52469145	chr11	449
293	cenRNA:chr20:27794182-27795173	chr20:27794182-27795173	chr20	991

294	cenRNA:chr19:26247238-26247657	chr19:26247238-26247657	chr19	419
295	cenRNA:chr11:53603618-53604218	chr11:53603618-53604218	chr11	600
296	cenRNA:chr11:53931742-53932704	chr11:53931742-53932704	chr11	962
297	cenRNA:chr1:122726785-122727112	chr1:122726785-122727112	chr1	327
298	cenRNA:chr1:124555142-124555592	chr1:124555142-124555592	chr1	450
299	cenRNA:chr12:35681712-35682253	chr12:35681712-35682253	chr12	541
300	cenRNA:chr11:51496033-51496453	chr11:51496033-51496453	chr11	420
301	cenRNA:chr5:48449166-48449862	chr5:48449166-48449862	chr5	696
302	cenRNA:chr11:52748519-52749461	chr11:52748519-52749461	chr11	942
303	cenRNA:chr17:23153815-23155037	chr17:23153815-23155037	chr17	1222
304	cenRNA:chr11:53525770-53526749	chr11:53525770-53526749	chr11	979
305	cenRNA:chr11:52391351-52392022	chr11:52391351-52392022	chr11	671
306	cenRNA:chr5:48647733-48648189	chr5:48647733-48648189	chr5	456
307	cenRNA:chr15:17537697-17538370	chr15:17537697-17538370	chr15	673
308	cenRNA:chr11:52347105-52348212	chr11:52347105-52348212	chr11	1107
309	cenRNA:chr12:35690131-35690774	chr12:35690131-35690774	chr12	643
310	cenRNA:chr5:49747416-49747904	chr5:49747416-49747904	chr5	488
311	cenRNA:chr9:44278748-44279361	chr9:44278748-44279361	chr9	613
312	cenRNA:chr1:123557258-123557685	chr1:123557258-123557685	chr1	427
313	cenRNA:chr17:24953969-24954553	chr17:24953969-24954553	chr17	584
314	cenRNA:chr11:51441676-51442072	chr11:51441676-51442072	chr11	396
315	cenRNA:chr1:123610460-123611045	chr1:123610460-123611045	chr1	585
316	cenRNA:chr15:19697940-19698368	chr15:19697940-19698368	chr15	428
317	cenRNA:chr1:124064764-124065161	chr1:124064764-124065161	chr1	397
318	cenRNA:chr11:52345163-52345592	chr11:52345163-52345592	chr11	429
319	cenRNA:chr20:28299579-28300135	chr20:28299579-28300135	chr20	556
320	cenRNA:chr1:122899028-122899394	chr1:122899028-122899394	chr1	366
321	cenRNA:chr3:93474763-93475288	chr3:93474763-93475288	chr3	525
322	cenRNA:chr17:25842790-25843442	chr17:25842790-25843442	chr17	652
323	cenRNA:chrX:61670116-61670515	chrX:61670116-61670515	chrX	399
324	cenRNA:chr20:27438283-27438650	chr20:27438283-27438650	chr20	367
325	cenRNA:chr19:25581321-25581621	chr19:25581321-25581621	chr19	300
326	cenRNA:chr4:49756355-49757298	chr4:49756355-49757298	chr4	943
327	cenRNA:chr11:51143036-51143500	chr11:51143036-51143500	chr11	464
328	cenRNA:chr11:52627854-52628287	chr11:52627854-52628287	chr11	433
329	cenRNA:chr11:53861602-53861971	chr11:53861602-53861971	chr11	369
330	cenRNA:chr3:92366738-92367270	chr3:92366738-92367270	chr3	532
331	cenRNA:chr19:24908795-24909492	chr19:24908795-24909492	chr19	697
332	cenRNA:chr1:123346957-123347459	chr1:123346957-123347459	chr1	502
333	cenRNA:chr20:28317146-28317550	chr20:28317146-28317550	chr20	404
334	cenRNA:chr11:51141091-51141561	chr11:51141091-51141561	chr11	470
335	cenRNA:chr17:23103073-23103511	chr17:23103073-23103511	chr17	438

336	cenRNA:chr4:49718514-49718886	chr4:49718514-49718886	chr4	372
337	cenRNA:chr11:54098805-54099144	chr11:54098805-54099144	chr11	339
338	cenRNA:chr5:49511240-49512044	chr5:49511240-49512044	chr5	804
339	cenRNA:chr11:53251143-53251818	chr11:53251143-53251818	chr11	675
340	cenRNA:chr11:54301082-54302262	chr11:54301082-54302262	chr11	1180
341	cenRNA:chr3:91658284-91658895	chr3:91658284-91658895	chr3	611
342	cenRNA:chr17:24692478-24692854	chr17:24692478-24692854	chr17	376
343	cenRNA:chr11:52737387-52737898	chr11:52737387-52737898	chr11	511
344	cenRNA:chr11:53825053-53825395	chr11:53825053-53825395	chr11	342
345	cenRNA:chr3:93230726-93231138	chr3:93230726-93231138	chr3	412
346	cenRNA:chr11:52990656-52991239	chr11:52990656-52991239	chr11	583
347	cenRNA:chr19:26458002-26458449	chr19:26458002-26458449	chr19	447
348	cenRNA:chr11:54237176-54238210	chr11:54237176-54238210	chr11	1034
349	cenRNA:chr1:124500811-124501365	chr1:124500811-124501365	chr1	554
350	cenRNA:chr11:52082783-52083338	chr11:52082783-52083338	chr11	555
351	cenRNA:chr7:59085472-59085993	chr7:59085472-59085993	chr7	521
352	cenRNA:chr11:54123668-54124051	chr11:54123668-54124051	chr11	383
353	cenRNA:chr17:23177999-23178489	chr17:23177999-23178489	chr17	490
354	cenRNA:chr17:23133938-23134784	chr17:23133938-23134784	chr17	846
355	cenRNA:chr11:52830623-52831542	chr11:52830623-52831542	chr11	919
356	cenRNA:chr11:53295221-53295856	chr11:53295221-53295856	chr11	635
357	cenRNA:chr10:41447011-41447647	chr10:41447011-41447647	chr10	636
358	cenRNA:chr11:52384360-52384961	chr11:52384360-52384961	chr11	601
359	cenRNA:chr11:53191148-53191571	chr11:53191148-53191571	chr11	423
360	cenRNA:chr16:38016735-38017158	chr16:38016735-38017158	chr16	423
361	cenRNA:chr11:54189530-54190313	chr11:54189530-54190313	chr11	783
362	cenRNA:chr7:59898072-59898749	chr7:59898072-59898749	chr7	677
363	cenRNA:chr3:92888929-92889860	chr3:92888929-92889860	chr3	931
364	cenRNA:chr12:35992710-35993895	chr12:35992710-35993895	chr12	1185
365	cenRNA:chr11:53304574-53305365	chr11:53304574-53305365	chr11	791
366	cenRNA:chr10:41493821-41494758	chr10:41493821-41494758	chr10	937
367	cenRNA:chr11:52614908-52615590	chr11:52614908-52615590	chr11	682
368	cenRNA:chr11:53637381-53637808	chr11:53637381-53637808	chr11	427
369	cenRNA:chr11:52778775-52780298	chr11:52778775-52780298	chr11	1523
370	cenRNA:chr12:36522876-36524738	chr12:36522876-36524738	chr12	1862
371	cenRNA:chr8:44594360-44595046	chr8:44594360-44595046	chr8	686
372	cenRNA:chr12:34998907-34999446	chr12:34998907-34999446	chr12	539
373	cenRNA:chr17:26270660-26271274	chr17:26270660-26271274	chr17	614
374	cenRNA:chr11:52806198-52806850	chr11:52806198-52806850	chr11	652
375	cenRNA:chr18:18528554-18528947	chr18:18528554-18528947	chr18	393
376	cenRNA:chr7:59669642-59670334	chr7:59669642-59670334	chr7	692
377	cenRNA:chr7:58378749-58379667	chr7:58378749-58379667	chr7	918

378	cenRNA:chr12:36531171-36533621	chr12:36531171-36533621	chr12	2450
379	cenRNA:chr18:15917121-15917555	chr18:15917121-15917555	chr18	434
380	cenRNA:chr11:54289548-54290286	chr11:54289548-54290286	chr11	738
381	cenRNA:chr2:94046568-94046928	chr2:94046568-94046928	chr2	360
382	cenRNA:chr11:51678914-51679313	chr11:51678914-51679313	chr11	399
383	cenRNA:chr17:24809917-24810585	chr17:24809917-24810585	chr17	668
384	cenRNA:chr3:91009604-91009965	chr3:91009604-91009965	chr3	361
385	cenRNA:chr17:26266579-26266979	chr17:26266579-26266979	chr17	400
386	cenRNA:chr3:93282114-93283208	chr3:93282114-93283208	chr3	1094
387	cenRNA:chr11:51528828-51529930	chr11:51528828-51529930	chr11	1102
388	cenRNA:chr16:36345826-36346773	chr16:36345826-36346773	chr16	947
389	cenRNA:chr20:28336851-28337254	chr20:28336851-28337254	chr20	403
390	cenRNA:chr5:49407661-49408105	chr5:49407661-49408105	chr5	444
391	cenRNA:chr20:27075758-27076203	chr20:27075758-27076203	chr20	445
392	cenRNA:chr11:53296905-53297311	chr11:53296905-53297311	chr11	406
393	cenRNA:chr20:28041136-28042216	chr20:28041136-28042216	chr20	1080
394	cenRNA:chr12:36366027-36366473	chr12:36366027-36366473	chr12	446
395	cenRNA:chr15:19095211-19095856	chr15:19095211-19095856	chr15	645
396	cenRNA:chr22:14910304-14910711	chr22:14910304-14910711	chr22	407
397	cenRNA:chr17:25597444-25598092	chr17:25597444-25598092	chr17	648
398	cenRNA:chr4:51235620-51235988	chr4:51235620-51235988	chr4	368
399	cenRNA:chr11:51276659-51277471	chr11:51276659-51277471	chr11	812
400	cenRNA:chr7:59793816-59794226	chr7:59793816-59794226	chr7	410
401	cenRNA:chr11:51176830-51177362	chr11:51176830-51177362	chr11	532
402	cenRNA:chr11:51798688-51799307	chr11:51798688-51799307	chr11	619
403	cenRNA:chr17:24882900-24883521	chr17:24882900-24883521	chr17	621
404	cenRNA:chr4:50608432-50609053	chr4:50608432-50609053	chr4	621
405	cenRNA:chr11:54094659-54095032	chr11:54094659-54095032	chr11	373
406	cenRNA:chr1:122933713-122934128	chr1:122933713-122934128	chr1	415
407	cenRNA:chr11:52670738-52671692	chr11:52670738-52671692	chr11	954
408	cenRNA:chr1:124754461-124754918	chr1:124754461-124754918	chr1	457
409	cenRNA:chr11:52868853-52869562	chr11:52868853-52869562	chr11	709
410	cenRNA:chr11:53922752-53923127	chr11:53922752-53923127	chr11	375
411	cenRNA:chr5:48471029-48471404	chr5:48471029-48471404	chr5	375
412	cenRNA:chr5:47565226-47565644	chr5:47565226-47565644	chr5	418
413	cenRNA:chr3:93151408-93152289	chr3:93151408-93152289	chr3	881
414	cenRNA:chrX:61063675-61064395	chrX:61063675-61064395	chrX	720
415	cenRNA:chr17:23206055-23206478	chr17:23206055-23206478	chr17	423
416	cenRNA:chr15:19059864-19060545	chr15:19059864-19060545	chr15	681
417	cenRNA:chr15:19433431-19433767	chr15:19433431-19433767	chr15	336
418	cenRNA:chr11:52647375-52647973	chr11:52647375-52647973	chr11	598
419	cenRNA:chr9:44436592-44437062	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

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51.2469	24.2789	48.3182	57.4155
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1.43677	1.78523	2.53221	2.4627
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2.74413	1.13704	4.37759	5.75126
2.85736	1.77519	0.359709	2.44885
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1.1758	0	1.7766	3.35967
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4.19155	0	4.22145	4.78984
1.06609	0	2.41646	0.609292
1.22422	1.52241	0.411316	0.700045
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2.06966	0	0.520831	2.36383
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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

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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
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1.51376	0	0	0.864835
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1.03108	0	0.779062	0.589304
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1.77764	1.10488	0.671649	1.01611
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1.32697	0	0	1.13796
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1.29684	0	0.653101	0.741036
1.49696	0	0.565662	0
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3.13927	0	0	0
2.16899	0	0	0
1.73967	0	0	0.993722
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1.71655	0	2.59253	1.96106
1.87608	0	0.709083	0
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2.38017	0	0.599581	0.90708
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1.40096	0	0.352939	1.60184
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1.66119	2.06372	0.418174	0.948955
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1.29802	0.538046	0.8722	0.742226
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1.18045	0	0	0
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1.74701	1.55201	0.817662	0.428194
1.37706	0.570906	0.694101	1.31259
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1.05269	0	0.265123	0
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1.14894	0	0	0.656602
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1.63998	2.0374	0.412842	0
2.13214	1.32588	0.604498	1.21936
1.14372	0	0.288028	0.653618
2.54143	0	0.959934	0.726121
1.90528	0	0.479527	0
1.03533	0	0	0
1.03108	0	0.259687	0.589304
1.89152	0	0.952137	1.08033
1.59686	0	0	1.82568
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
1.05269	0	0.79537	0
1.75145	0	0.440862	0
2.62744	0	0	0
3.47934	2.16107	0.437901	0.993722
1.20241	0	0.555577	0.802302
1.03533	0	0.78227	0.591731
2.05	1.69917	1.37722	1.56265
1.18199	0	0.893543	0.450601
1.02407	0	0.258029	0
2.03789	0	0.51285	0
2.24487	0.697826	0.141402	0.641761
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
1.82204	0	0	0.694483
1.07983	1.34211	0.271954	0
1.93337	2.40133	0	0
2.06122	0	0	0.392798
1.06307	0	0	0.911747
2.2499	0	0.70859	0.321598
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
1.02687	1.27634	0.517254	0
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
1.82537	0	0.459443	0

1.82537	0	0.918885	1.04261
2.10144	0	1.23529	0.800919
1.00631	0	0.253452	0.575154
2.38065	0.592068	0.71983	0.544499
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_In
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
5.14427	0	0.670006	5.14427	2.36363
5.14344	0.282591	2.44658	5.14344	0.799166
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	2.71017	0.484259
2.69817	0.464944	3.57807	2.71931	0.175314

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

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	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	2.11141	1.38954	0.165524
1.38618	0.109479	0.315945	1.92031	0.495371
1.38176	0.24944	1.07978	1.38176	0.141083

1.38167	0.349194	3.52707	1.53196	1.18502
1.37429	0	1.25294	1.90528	0.491124
1.37067	0.240565	0.694244	1.37067	0.380977
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	0.447259	2.71931	0.525943
1.21906	0.0592497	0.341976	2.07778	0.134046
1.21447	0.282705	0.932405	1.21447	0.54822

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

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_enri	shb_input_e	Delta_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	1.581	3.614	3.418	2.033
0.864704	1.88021	2.220	0.635	1.651	-1.585
1.6734	1.92429	2.594	0.287	0.538	-2.307
3.10463	4.58193	2.389	1.168	2.645	-1.222
0.486984	1.01817	2.282	0.003	0.534	-2.279
2.64452	3.09628	2.233	2.469	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	0.664	1.763	1.915	1.099
1.25202	0.698049	1.075	0.975	0.421	-0.099
2.16556	1.75448	1.097	1.582	1.171	0.486
2.05318	1.42393	0.961	1.323	0.694	0.362
1.09107	1.33361	1.098	0.813	1.055	-0.285
0.805401	0.673563	1.166	0.316	0.184	-0.850
0.619404	0.431677	0.942	-0.133	-0.321	-1.076
0.670518	2.99072	0.982	0.374	2.694	-0.608
2.60432	2.20913	0.937	1.790	1.395	0.853
1.6564	1.21211	0.957	0.950	0.506	-0.007
1.43318	1.11297	1.054	0.958	0.638	-0.096
1.62637	1.36014	0.974	1.430	1.164	0.456
0.964241	0.907203	1.088	0.645	0.588	-0.444
1.9838	2.02775	0.968	1.618	1.662	0.650
1.32226	2.65396	1.226	0.796	2.128	-0.430
0.202201	1.52192	1.160	0.068	1.388	-1.092
1.0337	0.749224	0.932	0.485	0.201	-0.446

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%
-2.636	-22.20%	-54.22%
-1.990	-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 α-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 HeLa 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 α-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 α-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 CENP-B 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 re-sequencing 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 alignment	Human genome reference hg19	No significant alignment : Shorter contiguous hit (20bp) than the longest contiguous hit in a random sequence of the same length and GC content (23bp)
BLAST alignment	Human transcript sequence	No significant alignment : With an average exon size of 123 bases (Scherer, 2008), unlike cenRNA#1 transcription from short exons separated by long introns
BLAST alignment	extended higher-order repeats from chromosome X from (2)	No significant alignment
BLAST alignment	hg38 reference assembly, incorporating several megabases of new centromeric assembly (https://genomereference.org)	No significant alignment
BLAST alignment	α-satellite monomers and novel repeating centromeric elements from (3)	No significant alignment
BLAST alignment	α-satellite monomers and novel repeating centromeric elements from (4)	No significant alignment
BLAST alignment	VecScreen	Some similarities with vector sequence
BLAST alignment	nr database	No significant alignment
BLAST alignment	small RNAs	No significant alignment
BLAST alignment	viral sequences	No significant alignment
BLAST alignment	HeLa genome (5,6)	No significant alignment

Supplemental Note - Table 2: List of databases and sequences questioned to identify cenRNA#1 origin

NCBI databases	-Human genome + transcript (Build 38) -Non-redundant nucleotide collection (nr/nt) -Expressed sequence tags (EST) -Genomic survey sequences (gss) -High-throughput genomic sequences (hgts) -Whole genome shotgun contigs (wgs) -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) -DRX001262: Hela cells (without wild-type U2AF35 induction by doxycycline) DRP000527 • RNA sequencing of wild-type or mutant U2AF35 transduced HeLa Cells -DRX002709: Chromatin immunoprecipitated DNA of CFIm68 in control Hela cells DRP000897 • Illumina sequencing of CFIm68 binding regions in Hela cells -DRX002710: Input DNA for CFIm68 ChIP of control Hela cells DRP000897 • Illumina sequencing of CFIm68 binding regions in Hela cells -DRX013196: HeLa PolII DRP001297 • Construction of Mate Pair Full-length cDNAs Libraries and Characterization of Transcriptional Start Sites and Termination Sites -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 -SRX749241: RnaSeq_HeLa_cell_RNaseRSRP049453 • Homo sapiens Transcriptome or Gene expression -SRX749316: RnaSeq_HeLa_cell_RibominusSRP049453 • Homo sapiens Transcriptome or Gene expression -ERX615573: Whole Genome Sequencing of human

	-SRX699196: whole genome sequence of HeLa cells: Sample JR6-UPL_ACTTGAStudy summary: SRP046745 • HeLa Genome sequencing -SRX699188: whole genome sequence of HeLa cells: Sample JR5-QPCR_CGTACG SRP046745 • HeLa Genome sequencing
dbGaP	-Epigenetic Profiling of Human Colorectal Cancer (phs000385.v1.p1) -HeLa Cell Genome Sequencing Studies (phs000640.v3.p1)
Specialized databases	-DASHR: database of small human noncoding RNAs (Leung, 2015) -deepBase v2.0 (Zhang, 2015) -EMBL Rfam database (Database of RNA family domains) -mIRbase -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	AGCCAACGGAATTCCTTTGGC	p2 (16/16 100%) a2 (11/11 100%)	chr10:3723839-3723855 (17/17 100%)
Region 2: 23bp	CGCGAATTCCAGCTAGTCCAGCC	p2 (18/18, 100%) a1 (12/12 100%)	chr11:96647943-96647960 (18/18, 100%) chr7:131446816-131446832 (17/17, 100%) chrX:24111144-24111160 (17/17 100%)
Region 3: 64bp	TCAGCCAACGGAATTCCTCACTAACCGCGAATTCCAGCTAGTCAGCCAACGGAATTCCAGCTAGT	p2 (23/23 100%) a2 (15/15 100%) multiple short hits	chr2:22737705- 22737730 (23/26, 88.5%)

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

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

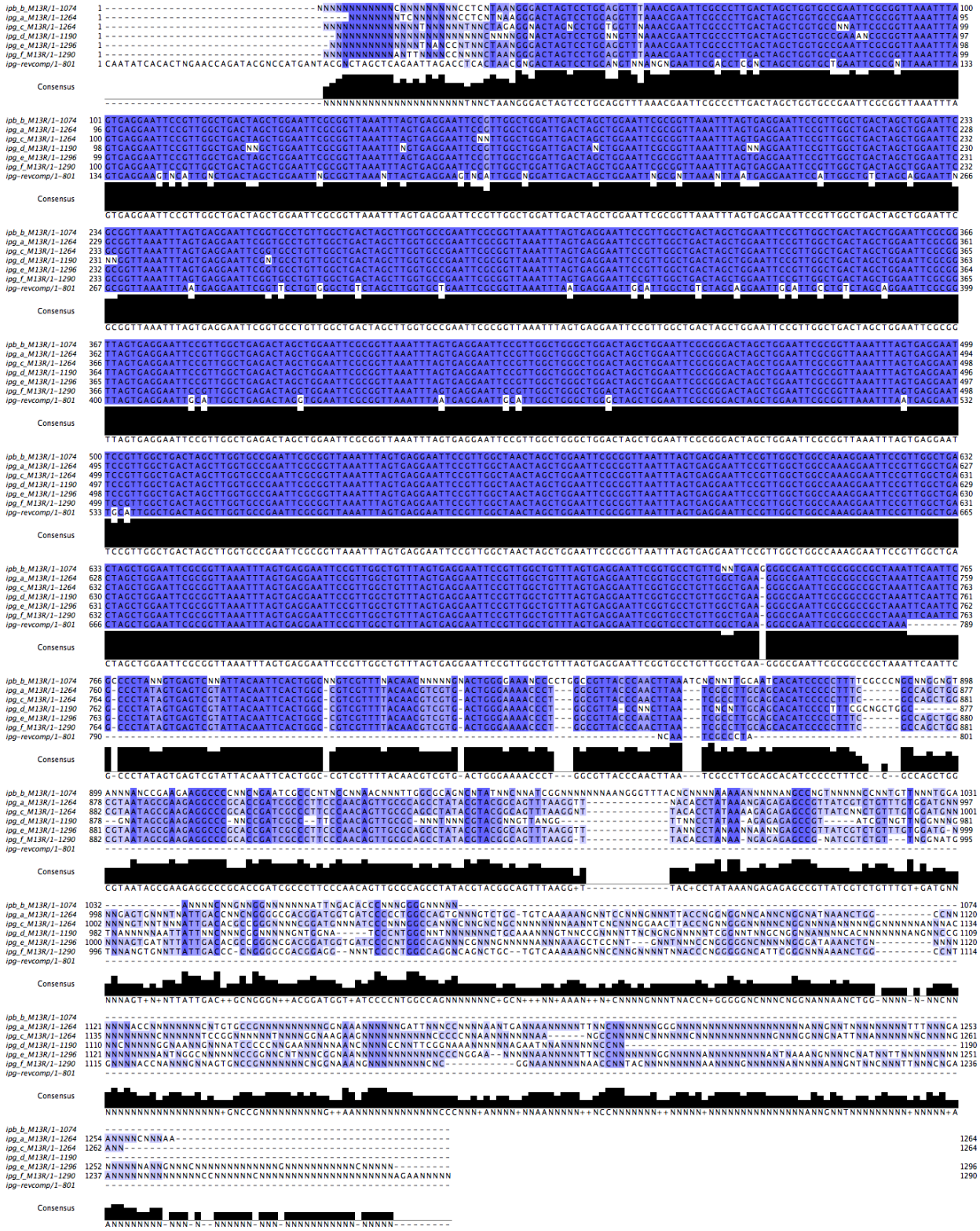
Supplemental Note - Table 5: Changes to cenRNA#1 shRNA sequence.

shRNA	Previous sequence	New sequence
shRNA-A	CAAGCTAGTCAGCCAA**T**G**C**AATTCCTCA**T**	CAAGCTAGTCAGCCAA**C**G**G**AATTCCTCA**C**
shRNA-B	**T**GCTAG**A**CAGCCAA**T**G**C**AATTCCTCA**T**TA	**A**GCTAG**T**CAGCCAA**C**G**G**AATTCCTCA**C**TA

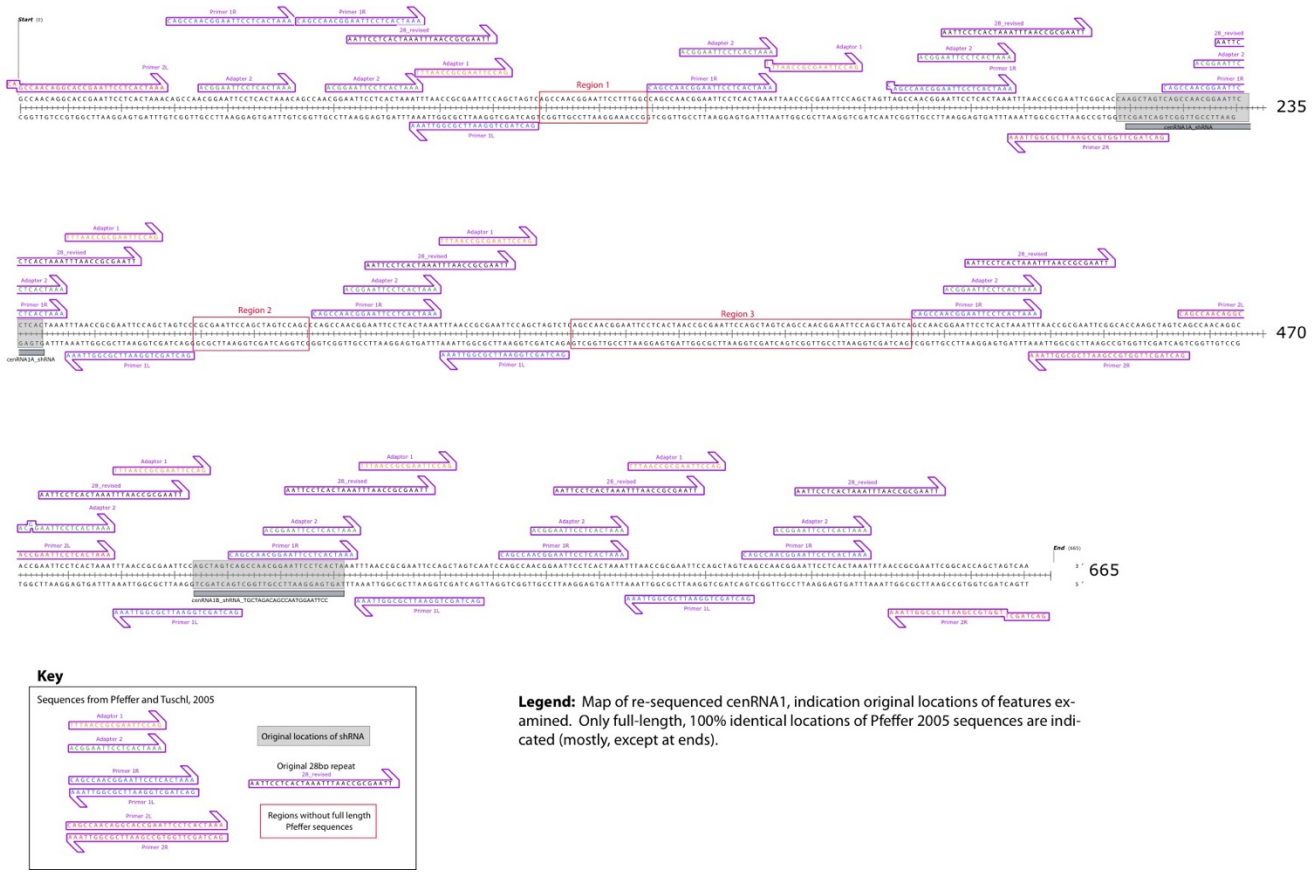
Supplemental Note - Table 6: Potential targeted lncRNA by cenRNA#1 shRNA.

Target	Alignment statistics
long intergenic non-protein coding RNA 971 (LINC00971)	Identities: 15/15 Query: ^{7} AGTCAGCCAACGGAA^{21} | | | | | | | | | | | | | | | Subject: ^{722} AGTCAGCCAACGGAA^{736}
Sequence ID: NR_033860.1	Length: 7319 (chr3: 84638405-84869575)

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 (~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).



Legend: Map of re-sequenced cenRNA1, indication original locations of features examined. Only full-length, 100% identical locations of Pfeffer 2005 sequences are indicated (mostly, except at 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 | aa)
ORF2	-	1	406	122	285 | 94

>lcl|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
236

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 | aa)
ORF1	+	1	184	480	297 | 98

>lcl|ORF1

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\

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 SNLNYQRKVQHCGLNANITKKVLRMLLFS-SVRFIPFPTKSSERPKYPLADPTDSVFPNC 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