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Supplemental Information

Persistence of RNA transcription

during DNA replication delays duplication

of transcription start sites until G2/M

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Figure S1. Genomic approaches to characterize transcription and replication together, Related to Figure 1

(A) Replication timing profiles from early to late S phase for the long arm of chromosome 7 shown in Fig 1B, and their reproducibility in two biological replicates. (B) Image adapted from Hansen et al., 2010, showing that our approach produces data similar to previously published Repli-Seq ones, but with higher resolution. (C) Representative western blotting analysis for the validation of the cellular fraction strategy in BJ-hTERT cells as in *Mayer et al.*, 2015. Subcellular localization markers were α -tubulin for cytoplasm (Cyt), U1 snRNP70 for nucleoplasm (Nuc) and histone H3 for chromatin (Chr), plus transcriptionally engaged Ser5-P RNAPII. (D) Timing of replication for actively transcribed genes (RPM>1). (E) Transcription levels in RPM and gene lengths of transcripts based on replication timing. (F) Single gene analysis of DNA replication levels from Fig 1C compared with the replication levels for the gene from the BrdU-Seq, calculated as reads per kilobase per million (RPKM) normalized to the Input, showing reproducible and consistent replication timing peak between the single gene and the BrdU-Seq analysis; n=3 for the BrdU IP, n=2 for the BrdU-Seq; average mean +/- SEM. (G) Nascent transcription levels presented as fold change (FC) relative to G1/S levels from Fig 1D; n=3; average mean +/- SEM; Student t-test. (H) Transcription activity measured by EU incorporation level followed by Clik-IT; asynchronous and serum starved released cells at the different timepoints are pulsed for 1h with EU before being fixed and analyzed by FACS. EU intensity is quantified for cells gated in G1 and G2 for DNA content and compared to EU incorporation levels in asynchronous growing cells. Average mean +/- Standard Deviation; Student t-test. (I) Procedure to derive reciprocal directionality between the leading replication fork and RNAPII transcription, with a specific example on chromosome (Chr) 7. DNA replication moves from replication origins to replication termination sites. Therefore, in a replication timing profile, the tip in the "inverted V" region (Hansen et al., 2010) will represent sites of replication initiation. Sites of replication termination will be instead where two consecutive "inverted V" converge in the replication timing profile. BrdU-Seq is not able to identify specifically DNA replication origins but the combination of all the timepoints together can identify regions where replication initiates. Highlighted in the figure as '1' '2' and '3' are three sites where replication initiates, numbered according to when these origins are activated along the S phase, from early to late. By knowing where the replication initiation sites are and as the leading replication fork progresses from 5' to 3' along the DNA, we can determine whether the leading replication fork is progressing along the Watson or the Crick strand across a specific region. By overlapping the directionality of the replication fork with that of the genes (from the TSS to the TTS), we can define the reciprocal directionality between the leading replication fork and the RNAPII. If both are moving in the same direction we define them as codirectional; if they move in opposite directions they are head to head; if they are in a combination of the two they are defined as transition, because of any of these i) the gene is replicated with replication forks entering from both ends; ii) a replication origin is activated inside the gene iii) the gene contains a replication termination site (see example of long gene in the bottom right, that contains both a replication origin and a replication termination site). Snapshot of the Chr-RNA-Seq data across the region is represented, to show that not all the transcripts present in the region are transcribed. (J) Frequency of codirectional, head to head and transition genes derived as from Fig S11. (K) Transcription levels and gene lengths of genes in Fig S1J based on their directionality; COD = codirectional; HtH = head to head; Trans = transition; box-whiskers plots with line at the median, MannWhitney t-test; test * => p-value < 0.05; ** => p-value < 0.01; *** => p-value < 0.001; **** => p-value < 0.0001.



Figure S2. Transcription shut down of genes when they get replicated, Related to Figure 2 (A) As for Fig 2A, relative fold changes of Chr-RNA-Seq levels of Early S replicated genes compared to G1/S and Early/Mid S, over the whole gene including exons. (B) As for Fig 2B for genes replicated in Early S shown in Fig 1D and being more transcribed throughout S/G2. (C-E) ChOR-Seq profiles for Ser5-RNAPII from *Stewart-Morgan et al., 2019* in nascent replicated chromatin, 1 h and 2 h after replication, centered around the TSS +/- 2.5 kb for (C) All Genes in the mouse genome, (D) genes > 100 kb, and (E) genes < 5 kb. (F) As for Fig 2A but for the Early/Mid S replicated genes, showing broader reduced transcription shut down compared to G1/S. (G) Gene length for genes that show a reduction of nascent transcription levels when they get replicated compared to all the other transcripts replicated in the same timepoint; Mann-Whitney t-test; **** => p-value < 0.0001; * => p-value < 0.05. (H) As for Fig 2F for all the genes replicated in each timepoint, comparing average profile in the timepoint they are replicated (during) with the one earlier (before).



Figure S3. TSS of transcribed genes are the only transcriptional pausing hotspots that affect globally DNA replication, Related to Figure 3

(A) As for Fig 3A but of Input and BrdU-Seq signals alone without normalization. (B) As for Fig 3A but with TSS of transcribed genes based on directionality according to Fig S1J. (C) Average metagene profile of BrdU-Seq levels of Early S normalized to Input DNA around the 5'-end of Exons +/- 2.5 kb from all genes and from transcribed genes separated based on their directionality according to Fig S1J. (D) Average metagene profile of BrdU-Seq levels of Early S normalized to Input DNA around the TTS +/- 2.5 kb of all genes, specifically transcribed genes or not transcribed genes. (E) Average metagene profile of BrdU-Seq levels normalized to Input DNA around enhancers mapped in RPE fibroblasts (Cherry et al. 2018) for all the timepoints. (F) An asynchronous population of BJ cells is pulsed for 30 min with BrdU before cells are sorted in 5 fractions based on their DNA content by Violet DNA. BrdU-Seq is then performed from each fraction and analyzed. (G) BrdU-Seq levels over the indicated genes in the 5 Repli-Seq fractions quantified as percentage of the fraction with the highest level; n=2; average mean +/- SEM. (H) As Fig 3A with BrdU levels across TSS +/- 2.5kb over genes replicated in the different timepoints from the 5 Repli-Seq fractions. (I) As Fig 3B of the BrdU-Seq level of the 5 Repli-Seq fractions over transcribed genes sorted by gene length. (J) EdU-Seq dataset reanalysis profile across transcribed and not transcribed genes in RPE fibroblasts and for All Genes in U2OS cells (Macheret et al., 2018). (K) Schematic on how P^3R^2 is computed, calculating the ratios of the GRO-Seq coverage from Li et al., 2018 in the region -50/+300 around the TSS and +300/+1000 after the TSS, for all the transcribed genes longer than 1 kb. Gene length for genes according to their P3R2, with genes ranked from the highest to the lowest P3R2 and divided in 5 groups of equal size; box whiskers plots with line at the median, Mann-Whitney t-test; **** => p-value < 0.0001. Profiles generated using the computational environment EaSeq (Lerdrup et al., 2016).



Figure S4. TSS of transcribed genes are sites of DNA synthesis in G2/M, Related to Figure 4

(A) Representative western blotting analysis of the siRNA of SUPT5H and NELFA in BJ cells with antibodies against SUPT5H and NELFA, α-tubulin is used as a loading control. (B) Representative image of the mitotic cells sorting strategy by FACS. Cells that are both in G2 by DNA content and pS10-H3 positive (highlighted in the box) are sorted followed by BrdU sequencing. (C) Average binned profile from TSS to TTS for G-MiDS specific BrdU-Seq across all transcribed genes. (D) Average binned profile from TSS to TTS for G-MiDS specific BrdU-Seq across G-MIDS hotspot genes upon for CTR siRNA and after siRNA of NELFA. (E) (left) Average metagene profile of BrdU-Seq levels normalized to Input DNA in all timepoints around the TSS +/- 2.5 kb for the 449 G-MiDS hotspot genes. (right) Relative enrichment for G-MIDS genes of BrdU-Seq levels of all the timepoints compared to the levels in Early S. (F) Snapshots with IGV of the G-MiDS sequencing files over the indicated G-MiDS hotspot TSS for BJ cells synchronized with Ro3306 (green), BJ cells in G2/M sorted from asynchronous cells (blue) and U2OS cells in G2/M sorted from asynchronous cells (red). Profiles generated using the computational environment EaSeq (*Lerdrup et al., 2016*).



Figure S5 Asymmetric replication fork progression from TSS associated replication origins, Related to Figure 5

(A) IGV snapshot of Repli-Seq profiles from the indicated fibroblasts cell lines, showing how the replication program from early (red) to late (blue) S-phase is conserved among fibroblasts. Data derived from http://www.replicationdomain.com (*Weddington et al., 2008*). (B) Average metagene profile for strand specific Ok-Seq from *Chen et al., 2019* +/- 2.5 kb around the TSS of G-MiDS hotspot genes, either on the '+' or the '-' strand. (C) As for (B) but specifically +/- 2.5 kb around the TSS of transcribed genes > 30 kb and < 100 kb in

BJ-hTERT. (D) Average metagene profile for strand specific Ok-Seq from *Chen et al., 2019* +/- 10 kb around the TTS of transcribed genes > 100 kb in BJ-hTERT, either on the '+' or the '-' strand (left panel), and with no strand specificity (right panel). (E) As for (D) +/- 10kb around enhancers identified in RPE cells as from *Cherry et al., 2018*. (F) As for Fig 5E specifically across the G-MiDS hotspots. Profiles generated using the computational environment EaSeq (*Lerdrup et al., 2016*).



Figure S6 DNA damage levels associated with G-MiDS, Related to Figure 6

(A) Read depth for the ChIP-Seq of RAD51, 53BP1 and XRCC4 in U2OS cells at the TSS +/- 10kb of all transcribed genes and only G-MiDS hotspots from from *Clouaire et al. 2018*. (B) Quantification of EdU foci positive mitotic cells following treatment for 16 h with 0.4 μM aphidicolin and Ro3306, released from the G2 arrest in medium containing EdU for 30 minutes in the presence of DMSO (CTR) or of 20 μM of Rad52 inhibitor (Rad52i). (C) Quantification of Rad51 foci positive cells in cells treated for 24 h with 1 μM of the PARP inhibitor Olaparib, treated in parallel either with DMSO (CTR) or with 25 μM Rad51 inhibitor (Rad51i).
(D) Comparison between EdU intensity of G2/M cells in cells untreated, or cells treated with 10 μM aphidicolin once released from the Ro3306 arrest; normal 'Low exposure' or equally amplified 'High exposure'.



Figure S7. BrdU gaps are dependent more generally on transcription and not only RNAPII; general features of G-MiDS hotspot genes and overlap with Cosmic Cancer Genes, Related to Figure 7

(A) Average metagene profile of BrdU-Seq levels of Early S normalized to Input DNA around the TSS +/- 2.5 kb for all transcribed genes and transcripts separated by gene length in CTR siRNA and after the siRNA of SUPT5H. (B) Average metagene profile of BrdU-Seq levels of Early S normalized to Input DNA around the TSS +/- 2.5 kb in DMSO and cells treated for 1 h with the indicated concentrations of triptolide while being pulsed with BrdU; plots are for transcribed genes separated by gene length. (C) Fold changes in the transcription levels of G-MiDS hotspot genes compared to the G1/S Chr-RNA-Seq timepoint throughout all other timepoints. (D) Average metagene profile of GRO-Seq levels around the TSS +/- 2.5kb of all genes in the human genomes for sense and antisense transcription, in control (CTR) cells and cells after the RNAi of NELFB and NELFE; data derived from Liu et al., 2017. (E) Average metagene profile of BrdU-Seq levels of Early S normalized to Input DNA of genes according to promoter class based on GC richness and GC skew as defined in Ginno et al., 2013. (F-G) (F) Gene length and (G) and transcription levels for genes based on their promoter class as defined in Ginno et al., 2013. (H) Quantification of Cap-Seq levels from Tan-Wong et al., 2019 at the TSS +/- 1 kb in a strand specific manner across ALL the transcribed genes in BJ-hTERT cells and only the G-MiDS hotspots, as fold change (FC) after the overexpression (OE) of RNASEH1. Only genes with a quantification for both sense and antisense transcription have been analyzed; Mann-Whitney t-test; **** => p-value < 0.0001, ns = not significative. (I) List of the G-MiDS hotspot genes identified in the COSMIC database as Cancer Genes, in particular genes with copy number alterations and/or sites of translocations.

Table S1: Gene ontology analysis of transcripts transcribed in the first time point at the G1/S transition, using the online DAVID Bioinformatic Resources (https://david.ncifcrf.gov), with DNA replication highlighted in bold. Related to Figure 1

GO Term	Counts	p-Value	Benjamini
transcription, DNA-templated	1413	1.50E-42	1.40E-38
cell division	304	2.00E-31	9.60E-28
cell-cell adhesion	244	9.80E-31	3.10E-27
rRNA processing	198	6.90E-29	1.60E-25
mitotic nuclear division	221	2.20E-26	4.10E-23
DNA repair	211	3.00E-26	4.70E-23
mRNA splicing, via spliceosome	200	2.30E-25	3.20E-22
proteasome-mediated ubiquitin-dependent protein catabolic process	183	2.50E-23	3.00E-20
protein transport	322	4.20E-23	4.40E-20
regulation of transcription, DNA-templated	1051	1.10E-22	1.00E-19
cellular response to DNA damage stimulus	185	5.70E-22	4.90E-19
translation	218	9.50E-22	7.50E-19
DNA replication	144	1.50E-21	1.10E-18

Table S2: Gene ontology analysis of transcripts changing +/-2 Fold Change expression compared to the first time point at the G1/S transition, using the online DAVID Bioinformatic Resources (https://david.ncifcrf.gov). Related to Figure 1.

Term	Count	%	P-Value	Benjamini	
nucleosome assembly	7	15.2	1.10E-07	2.60E-05	16h UP
telomere organization	4	8.7	2.00E-05	2.40E-03	52 transcripts
DNA replication-dependent nucleosome assembly	4	8.7	3.30E-05	2.70E-03	
chromatin sliencing at rDNA	4	8./ 9.7	5.10E-05	3.10E-03	
	4	9.7	1.30E-03	5.70L-03	
negative regulation of gene expression, epigenetic	4	8.7	2 40E-04	8.40E-03	
gene silencing by RNA	4	87	1 30F-03	4 00F-02	
cellular protein metabolic process	4	8.7	1.60E-03	4.20E-02	
mitochondrial electron transport, NADH to ubiquinone	3	6.5	4.20E-03	9.70E-02	
	25	19.0	8 70E 30	5 70E 27	10h UD
telomere organization	14	10.5	2.80E-22	9 30E-20	147 transcripts
DNA replication-dependent nucleosome assembly	14	10.6	4 80F-21	1.00E-18	
chromatin silencing at rDNA	14	10.6	4.70E-20	7.80E-18	
protein heterotetramerization	14	10.6	3.30E-19	4.40E-17	
negative regulation of gene expression, epigenetic	14	10.6	4.40E-18	4.80E-16	
positive regulation of gene expression, epigenetic	14	10.6	9.60E-17	1.00E-14	
gene silencing by RNA	14	10.6	2.70E-13	2.30E-11	
cellular protein metabolic process	14	10.6	6.10E-13	4.50E-11	
regulation of gene silencing	7	5.3	2.80E-11	1.80E-09	
chromatin silencing	9	6.8	4.00E-10	2.40E-08	
	7	5.3	1.10E-09	3.90E-06	ł
DNA replication-independent nucleosome assembly	7	5.3	1.30E-09	2.90E-07	
DNA replication-independent nucleosome assembly	7	5.3	1.00E-08	4.50E-06	
double-strand break repair via nonhomologous end joining	8	6.1	1.50E-07	6.40E-06	
CENP-A containing nucleosome assembly	7	5.3	3.10E-07	1.20E-05	
beta-catenin-TCF complex assembly	7	5.3	3.10E-07	1.20E-05	
innate immune response in mucosa	5	3.8	1.80E-05	6.80E-04	
blood coagulation	9	6.8	2.50E-05	8.60E-04	
mitotic nuclear division	10	7.6	3.20E-05	1.00E-03	
antibacterial humoral response	5	3.8	1.80E-04	5.70E-03	
defense response to Gram-positive bacterium	6	4.5	2.20E-04	6.50E-03	
cell division	10	7.6	4.30E-04	1.20E-02	
cell division	42	17	3.60E-29	3.10E-26	22h UP
nucleosome assembly	28	11.3	2.50E-27	1.10E-24	299 transcripts
mitotic nuclear division	33	13.4	3.80E-24	1.10E-21	
telomere organization	14	5.7	1.10E-18	2.20E-16	
DNA replication-dependent nucleosome assembly	14	5.7	1.70E-17	2.90E-15	
chromatin silencing at rDNA	14	5.7 6.1	1.70E-16	5.10E-14	
notein beterotetramerization	10	5.7	4.30E-10	1 20E-13	
chromosome segregation	16	6.5	2.00E-15	1.90E-13	
sister chromatid cohesion	18	7.3	4.20E-15	3.60E-13	
positive regulation of gene expression, epigenetic	14	5.7	3.10E-13	2.40E-11	
gene silencing by RNA	14	5.7	6.70E-10	4.70E-08	
regulation of gene silencing	7	2.8	1.10E-09	7.30E-08	
cellular protein metabolic process	14	5.7	1.40E-09	8.70E-08	
CENP-A containing nucleosome assembly	10	4	1.50E-09	8.60E-08	
chromatin silencing	10	4	2.40E-09	1.20E-07	
mitotic sister chromatid segregation	8	3.2	1.20E-08	5.90E-07	
metanhase plate congression	6	2.0	4.20E-08	7 30E-06	
telomere capping	7	2.4	2 20F-07	9.30E-06	
anaphase-promoting complex-dependent catabolic process	10	4	3.90E-07	1.60E-05	
DNA replication-independent nucleosome assembly	7	2.8	4.90E-07	1.90E-05	
regulation of attachment of spindle microtubules to kinetochore	5	2	6.50E-07	2.40E-05	
spindle organization	6	2.4	8.70E-07	3.10E-05	
attachment of spindle microtubules to kinetochore	5	2	2.30E-06	7.80E-05	
positive regulation of ubiquitin protein ligase activity	5	2	2.30E-06	7.80E-05	
DNA-templated transcription, initiation	7	2.8	3.70E-06	1.20E-04	
mitotic metaphase plate congression	0	2.8	4.40E-06	1.40E-04	
G2/M transition of mitotic cell cycle	11	4.5	540F-06	1.60E-04	1
double-strand break repair via nonhomologous end ioining	8	3.2	9.30E-06	2.60E-04	
innate immune response in mucosa	6	2.4	9.70E-06	2.70E-04	1
beta-catenin-TCF complex assembly	7	2.8	1.10E-05	2.90E-04	
mitotic cytokinesis	6	2.4	2.10E-05	5.40E-04	
mitotic spindle organization	6	2.4	2.50E-05	6.20E-04	
regulation of chromosome segregation	4	1.6	8.80E-05	2.10E-03	
regulation of mitotic spindle organization	4	1.6	8.80E-05	2.10E-03	
mitotic spindle midzone assembly	4	1.6	8.80E-05	2.10E-03	
regulation of cell cycle	9	3.0 6.1	1.20E-04	2.70E-03	l
	1 10	1 0.1			1

regulation of ubiquitin-protein ligase activity involved in mitotic cell cycle	5	2	1.40E-04	3.10E-03	
antibacterial humoral response	6	2.4	1.70E-04	3.60E-03	
regulation of mitotic nuclear division	5	2	1.70E-04	3.60E-03	
cytokinesis	6	2.4	2.50E-04	5.20E-03	
protein ubiquitination involved in ubiquitin-dependent protein catabolic	9	3.6	4 80F-04	9 70E-03	
process	-	0.0		0.102 00	
defense response to Gram-positive bacterium	/	2.8	5.20E-04	1.00E-02	
positive regulation of cytokinesis	5	2	9.30E-04	1.80E-02	
regulation of meiotic nuclear division	3	1.2	1.40E-03	2.50E-02	
free ubiquitin chain polymerization	3	1.2	1.40E-03	2.50E-02	
negative regulation of ubiquitin-protein ligase activity involved in mitotic	6	2.4	1.50E-03	2.80E-02	
		1.0	4.005.00	0.005.00	
mitotic spindle assembly checkpoint	4	1.6	1.60E-03	2.90E-02	
nomologous chromosome segregation	3	1.2	2.00E-03	3.50E-02	
positive regulation of ubiquitin-protein ligase activity involved in regulation	6	2.4	2.10E-03	3.50E-02	
of mitolic cell cycle transition	c	2.4	2.005.02	4 905 00	
retrograde vesicle-mediated transport, Goigi to ER	0	2.4	2.90E-03	4.00E-02	
	3	1.2	3.70E-03	6.00E-02	
cell cycle	9	3.0	4.40E-03	0.90E-02	
	6	2.4	4.80E-03	7.30E-02	
regulation of mitotic metaphase/anaphase transition	3	12	4 80E-03	7 20E-02	
protein localization to kinetochore	3	1.2	5.90E-03	8 70E-02	
microtubule depolymerization	3	1.2	5.90E-03	8 70E-02	
DNA damage response signal transduction by p53 class mediator	Ŭ	1.2	0.002 00	0.102 02	
resulting in cell cycle arrest	5	2	6.20E-03	9.00E-02	
blood coagulation	8	3.2	6.40E-03	9.10E-02	1
	-	45.0	0.005.00	4.505.00	0.4h UD
	49	15.3	3.90E-32	4.50E-29	24n UP
nucleosome assembly	32	10	7.20E-30	4.10E-27	382 transcripts
	40	12.5	1.90E-28	7.30E-26	
telomere organization	15	4.7	4.00E-19	1.20E-16	
DNA replication-dependent nucleosome assembly	15	4.7	8.80E-18	2.00E-15	
sister chromatid cohesion	21	6.5	6.40E-17	2.10E-14	
chromatin silencing at rDNA	15	4./	1.10E-16	1.80E-14	
negative regulation of gene expression, epigenetic	16	5	4.70E-16	6.30E-14	
	15	4.7	8.50E-16	1.10E-13	
chromosome segregation	17	5.3	3.60E-15	4.10E-13	
positive regulation of gene expression, epigenetic	15	4.7	3.70E-13	3.80E-11	
	10	5			
gene silencing by RNA	10	0	1.30E-10	1.202 00	
gene silencing by RNA mitotic cytokinesis	10	3.1	2.90E-10	2.50E-08	
gene silencing by RNA mitotic cytokinesis CENP-A containing nucleosome assembly	10 10 11	3.1 3.4	2.90E-10 6.80E-10	2.50E-08 5.50E-08	
gene silencing by RNA mitotic cytokinesis CENP-A containing nucleosome assembly G2/M transition of mitotic cell cycle	10 10 11 16 15	3.1 3.4 5	1.30E-10 2.90E-10 6.80E-10 2.60E-09 3.10E.09	2.50E-08 5.50E-08 2.00E-07 2.20E-07	
gene silencing by RNA mitotic cytokinesis CENP-A containing nucleosome assembly G2/M transition of mitotic cell cycle cellular protein metabolic process	10 10 11 16 15	3.1 3.4 5 4.7	1.30E-10 2.90E-10 6.80E-10 2.60E-09 3.10E-09	2.50E-08 5.50E-08 2.00E-07 2.20E-07 3.20E-07	
gene silencing by RNA mitotic cytokinesis CENP-A containing nucleosome assembly G2/M transition of mitotic cell cycle cellular protein metabolic process negative regulation of megakaryocyte differentiation regulation of gene silencing	10 11 16 15 8 7	3.1 3.4 5 4.7 2.5 2.2	1.30E-10 2.90E-10 6.80E-10 2.60E-09 3.10E-09 4.70E-09	2.50E-08 5.50E-08 2.00E-07 2.20E-07 3.20E-07 3.20E-07	
gene silencing by RNA mitotic cytokinesis CENP-A containing nucleosome assembly G2/M transition of mitotic cell cycle cellular protein metabolic process negative regulation of megakaryocyte differentiation regulation of gene silencing chromatic silencing	10 11 16 15 8 7	3.1 3.4 5 4.7 2.5 2.2 3.1	1.30E-10 2.90E-10 6.80E-10 2.60E-09 3.10E-09 4.70E-09 5.00E-09 2.10E-08	2.50E-08 5.50E-08 2.00E-07 2.20E-07 3.20E-07 3.20E-07 1.20E-06	
gene silencing by RNA mitotic cytokinesis CENP-A containing nucleosome assembly G2/M transition of mitotic cell cycle cellular protein metabolic process negative regulation of megakaryocyte differentiation regulation of gene silencing chromatin silencing ananhase-promoting complex-dependent catabolic process	10 11 16 15 8 7 10 12	3.1 3.4 5 4.7 2.5 2.2 3.1 3.7	1.30E-10 2.90E-10 6.80E-10 2.60E-09 3.10E-09 4.70E-09 5.00E-09 2.10E-08 2.90E-08	2.50E-08 5.50E-08 2.00E-07 2.20E-07 3.20E-07 3.20E-07 1.20E-06 1.70E-06	
gene silencing by RNA mitotic cytokinesis CENP-A containing nucleosome assembly G2/M transition of mitotic cell cycle cellular protein metabolic process negative regulation of megakaryocyte differentiation regulation of gene silencing chromatin silencing anaphase-promoting complex-dependent catabolic process telomere capping	10 11 16 15 8 7 10 12 8	3.1 3.4 5 4.7 2.5 2.2 3.1 3.7 2.5	1.30E-10 2.90E-10 6.80E-10 2.60E-09 3.10E-09 4.70E-09 5.00E-09 2.10E-08 2.90E-08 3.40E-08	2.50E-08 5.50E-08 2.00E-07 2.20E-07 3.20E-07 3.20E-07 1.20E-06 1.70E-06	
gene silencing by RNA mitotic cytokinesis CENP-A containing nucleosome assembly G2/M transition of mitotic cell cycle cellular protein metabolic process negative regulation of megakaryocyte differentiation regulation of gene silencing chromatin silencing anaphase-promoting complex-dependent catabolic process telomere capping microtubula-based movement	10 11 16 15 8 7 10 12 8 12	3.1 3.4 5 4.7 2.5 2.2 3.1 3.7 2.5 3.7	1.30E-10 2.90E-10 6.80E-10 3.10E-09 4.70E-09 5.00E-09 2.10E-08 2.90E-08 3.40E-08	2.50E-08 2.50E-08 2.00E-07 2.20E-07 3.20E-07 3.20E-07 1.20E-06 1.70E-06 1.90E-06	
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gene silencing by RNA mitotic cytokinesis CENP-A containing nucleosome assembly G2/M transition of mitotic cell cycle cellular protein metabolic process negative regulation of megakaryocyte differentiation regulation of gene silencing chromatin silencing anaphase-promoting complex-dependent catabolic process telomere capping microtubule-based movement innate immune response in mucosa mitotic sister chromatid segregation mitotic sister chromatid segregation mitotic sister chromatid segregation DNA replication-independent nucleosome assembly beta-catenin-TCF complex assembly mitotic spindle organization DNA-templated transcription, initiation regulation of attachment of spindle microtubules to kinetochore antibacterial humoral response double-strand break repair via nonhomologous end joining defense response to Gram-positive bacterium positive regulation of ubiquitin protein ligase activity cytokinesis protein localization to kinetochore regulation of mitotic nuclear division cell division mitotic nuclear division nucleosome assembly telomere organization DNA replication-to kinetochore regulation of mitotic nuclear division cell division mitotic nuclear division nucleosome assembly telomere organization DNA replication-dependent nucleosome assembly protein heterotetramerization negative regulation of gene expression, epigenetic chromatin silencing at rDNA	$\begin{array}{c} 10 \\ 10 \\ 11 \\ 16 \\ 15 \\ 8 \\ 7 \\ 10 \\ 12 \\ 8 \\ 12 \\ 8 \\ 12 \\ 8 \\ 12 \\ 8 \\ 9 \\ 7 \\ 8 \\ 9 \\ 7 \\ 8 \\ 9 \\ 7 \\ 8 \\ 9 \\ 9 \\ 8 \\ 6 \\ 6 \\ 8 \\ 5 \\ 8 \\ 9 \\ 9 \\ 10 \\ 5 \\ 8 \\ 6 \\ 6 \\ 6 \\ 6 \\ 6 \\ 6 \\ 6 \\ 6 \\ 6$	3.1 3.4 5 4.7 2.5 3.1 3.7 2.5 2.8 2.2 2.5 2.8 2.5 2.8 2.5 2.8 2.5 2.8 2.5 1.9 2.5 1.6 2.5 1.6 2.5 1.6 2.5 1.6 2.5 1.6 2.5 1.6 2.5 1.6 2.5 1.6 2.5 1.6 2.5 1.6 2.5 1.6 2.5 3.1 1.6 2.5 1.6 2.1 2.3 2 2.1 2.3 2 <t< td=""><td>1.50E-10 2.90E-10 6.80E-10 2.60E-09 3.10E-09 4.70E-09 5.00E-09 2.10E-08 2.90E-08 3.40E-08 3.40E-08 3.40E-08 3.80E-08 6.50E-08 6.70E-08 8.20E-08 8.20E-08 8.20E-08 6.70E-08 8.20E-08 6.70E-07 9.80E-07 9.80E-06 6.620E-06 7.40E-06 1.00E-05 2.70E-24 8.50E-23 1.60E-11 1.60E-11</td><td>1.202.00 2.50E-08 5.50E-08 2.20E-07 2.20E-07 3.20E-07 3.20E-07 1.20E-06 1.70E-06 1.70E-06 3.20E-05 3.70E-05 4.20E-04 3.10E-04 6.30E-04 6.30E-04 1.30E-16 4.40E-11 9.50E-11 5.90E-10 2.70E-09 3.30E-09 3.30E-09 3.30E-09</td><td>28h UP 874 transcripts</td></t<>	1.50E-10 2.90E-10 6.80E-10 2.60E-09 3.10E-09 4.70E-09 5.00E-09 2.10E-08 2.90E-08 3.40E-08 3.40E-08 3.40E-08 3.80E-08 6.50E-08 6.70E-08 8.20E-08 8.20E-08 8.20E-08 6.70E-08 8.20E-08 6.70E-07 9.80E-07 9.80E-06 6.620E-06 7.40E-06 1.00E-05 2.70E-24 8.50E-23 1.60E-11 1.60E-11	1.202.00 2.50E-08 5.50E-08 2.20E-07 2.20E-07 3.20E-07 3.20E-07 1.20E-06 1.70E-06 1.70E-06 3.20E-05 3.70E-05 4.20E-04 3.10E-04 6.30E-04 6.30E-04 1.30E-16 4.40E-11 9.50E-11 5.90E-10 2.70E-09 3.30E-09 3.30E-09 3.30E-09	28h UP 874 transcripts
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gene silencing by RNA mitotic cytokinesis CENP-A containing nucleosome assembly G2/M transition of mitotic cell cycle cellular protein metabolic process negative regulation of megakaryocyte differentiation regulation of gene silencing chromatin silencing anaphase-promoting complex-dependent catabolic process telomere capping microtubule-based movement innate immune response in mucosa mitotic sister chromatid segregation mitotic sister chromatid segregation mitotic metaphase plate congression spindle organization DNA replication-independent nucleosome assembly beta-catenin-TCF complex assembly mitotic spindle organization DNA-templated transcription, initiation regulation of attachment of spindle microtubules to kinetochore antibacterial humoral response double-strand break repair via nonhomologous end joining defense response to Gram-positive bacterium positive regulation of ubiquitin-protein ligase activity cytokinesis protein localization to kinetochore regulation of mitotic nuclear division ficel division mitotic nuclear division ficel division mitotic nuclear division ficel nuclear division nucleosome assembly telomere organization sister chromatid cohesion DNA replication-dependent nucleosome assembly protein heterotetramerization negative regulation of gene expression, epigenetic chromosome segregation	$\begin{array}{c} 10 \\ 11 \\ 16 \\ 15 \\ 8 \\ 7 \\ 10 \\ 12 \\ 8 \\ 12 \\ 8 \\ 12 \\ 8 \\ 12 \\ 8 \\ 9 \\ 7 \\ 8 \\ 9 \\ 7 \\ 8 \\ 9 \\ 7 \\ 8 \\ 9 \\ 7 \\ 8 \\ 9 \\ 7 \\ 8 \\ 9 \\ 7 \\ 8 \\ 9 \\ 7 \\ 8 \\ 9 \\ 7 \\ 8 \\ 9 \\ 7 \\ 8 \\ 9 \\ 7 \\ 8 \\ 9 \\ 7 \\ 8 \\ 9 \\ 10 \\ 5 \\ 8 \\ 5 \\ 6 \\ 6 \\ 6 \\ 6 \\ 6 \\ 15 \\ 25 \\ 15 \\ 16 \\ 17 \\ 15 \\ 25 \\ 15 \\ 16 \\ 17 \\ 15 \\ 24 \\ 18 \\ \end{array}$	3.1 3.4 5 4.7 2.5 3.1 3.4 5 4.7 2.5 3.7 2.5 3.7 2.5 2.8 2.2 2.5 2.8 2.5 2.8 2.5 1.9 2.5 1.6 2.5 1.6 2.5 1.6 2.5 3.1 1.6 2.5 1.6 2.5 1.6 2.5 3.1 1.6 2.5 1.6 1.9 8.1 6.6 4.4 2 3.3 2 2.1 2.3 2.4	1.30E-10 2.90E-10 6.80E-10 2.60E-09 3.10E-09 4.70E-09 5.00E-09 2.10E-08 2.90E-08 3.40E-08 3.40E-08 3.40E-08 6.50E-08 6.50E-08 6.70E-08 8.20E-08 8.20E-08 8.20E-08 8.20E-08 8.20E-07 2.60E-07 9.80E-07 1.80E-06 4.10E-06 4.10E-06 4.20E-08 2.00E-05 2.10E-05 2.60E-05 2.70E-24 8.50E-12 1.10E-11 1.60E-11 1.60E-11 1.60E-11 3.30E-11 2.00E-10	1.202-06 2.50E-08 5.50E-08 2.00E-07 2.20E-07 3.20E-07 3.20E-07 1.20E-06 1.70E-06 1.70E-06 2.00E-06 3.20E-05 3.70E-05 6.50E-05 1.50E-04 1.50E-04 3.10E-04 6.30E-04 6.30E-04 6.30E-04 6.30E-04 5.90E-11 5.90E-11 5.90E-11 5.90E-10 2.70E-09 3.30E-09 4.40E-08	28h UP 874 transcripts
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CENP-A containing nucleosome assembly	12	1.6	2.60E-07	4.30E-05	
mitotic cytokinesis	10	1.3	5.30E-07	8.30E-05	
spindle organization	8	11	6 80E-07	1 00F-04	
ananhase-promoting complex-dependent catabolic process	15	2	8 10E-07	1 10E-04	
	7	2	0.102 07		
regulation of gene silencing	/	0.9	0.70E-07	1.10E-04	
retrograde vesicle-mediated transport, Golgi to ER	15	2	1.30E-06	1.60E-04	
metaphase plate congression	7	0.9	1.70E-06	2.00E-04	
mitotic sister chromatid segregation	9	1.2	1.80E-06	2.00E-04	
negative regulation of megakaryocyte differentiation	8	11	1 80E-06	1 90E-04	
antihesterial humanal reasonance	11	1.1	1.00E 00	2.005.04	
	11	1.5	2.90E-00	3.00E-04	
chromatin silencing	11	1.5	3.60E-06	3.60E-04	
mitotic metaphase plate congression	10	1.3	5.10E-06	4.80E-04	
gene silencing by RNA	16	2.1	1.10E-05	1.00E-03	
regulation of ubiguitin-protein ligase activity involved in mitotic cell cycle	8	11	1 20E-05	1.00E-03	
tolomore copping	8	1.1	1.20E 05	1.00E 03	
	0	1.1	1.20L-03	1.002-03	
innate immune response in mucosa	8	1.1	2.10E-05	1.80E-03	
DNA replication-independent nucleosome assembly	8	1.1	2.80E-05	2.30E-03	
negative regulation of ubiquitin-protein ligase activity in mitotic cell cycle	12	1.6	4.60E-05	3.60E-03	
defense response to Gram-positive bacterium	13	1.7	5.40E-05	4.10E-03	
regulation of attachment of spindle microtubules to kinetochore	5	0.7	5 50E-05	4 00E-03	
mitation of attachment of spinale microtabales to kinetochore	0	1.1	7.000 05	F.COE 00	
	0	1.1	7.60E-05	5.00E-03	
positive regulation of ubiquitin-protein ligase activity involved in regulation	12	16	8 60E-05	6 00E-03	
of mitotic cell cycle transition	L .=				
beta-catenin-TCF complex assembly	9	1.2	1.30E-04	9.00E-03	
microtubule-based movement	12	1.6	1.60E-04	1.00E-02	
regulation of mitotic nuclear division	7	0.9	1 70F-04	1 10E-02	i
	5	0.3	1.00-04	1 100 02	1
positive regulation of ubiquitin protein ligase activity	5	0.7	1.90E-04	1.10E-02	
DNA-templated transcription, initiation	8	1.1	2.60E-04	1.60E-02	
protein localization to kinetochore	5	0.7	3.00E-04	1.80E-02	
protein K11-linked ubiquitination	7	0.9	3.40E-04	1.90E-02	
mitochondrial ATP synthesis coupled proton transport	6	0.8	7 70E-04	1 20E-02	
nitochondrial Arr synthesis coupled proton transport	5	0.0	0.405.04	4.20L-02	
positive regulation of 1 cell mediated cytotoxicity	5	0.7	9.40E-04	5.00E-02	
negative regulation of cell proliferation	28	3.7	1.30E-03	6.70E-02	
cytokinesis	8	1.1	1.60E-03	8.10E-02	
mitotic chromosome condensation	5	07	1 70F-03	8 30E-02	
DNA damage response, signal transduction by p53 class mediator	-				
regulting in cell cycle errort	9	1.2	1.70E-03	8.20E-02	
	10	4.0	4 005 00	0 00 - 00	
cell redox homeostasis	10	1.3	1.80E-03	8.60E-02	
cell proliferation	26	3.4	1.90E-03	8.60E-02	
double-strand break repair via nonhomologous end joining	9	1.2	1.90E-03	8.60E-02	
	0	10	0.405.00	0.005.00	
type Linterferon signaling pathway	9	1.4	2.10E-03	9.30E-02	
type I interferon signaling pathway	9	1.2	2.10E-03	9.30E-02 9.50E-02	
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling	9 15	2	2.10E-03 2.20E-03	9.30E-02 9.50E-02	
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation	9 15 4	2 0.5	2.10E-03 2.20E-03 2.30E-03	9.30E-02 9.50E-02 9.80E-02	
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly	9 15 4 4	1.2 2 0.5 0.5	2.10E-03 2.20E-03 2.30E-03 2.30E-03	9.30E-02 9.50E-02 9.80E-02 9.80E-02	
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly	9 15 4 4	1.2 2 0.5 0.5	2.10E-03 2.20E-03 2.30E-03 2.30E-03	9.30E-02 9.50E-02 9.80E-02 9.80E-02	
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly	9 15 4 4	0.5 0.5	2.10E-03 2.20E-03 2.30E-03 2.30E-03	9.30E-02 9.50E-02 9.80E-02 9.80E-02	16h DOWN
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment	9 15 4 4	1.2 2 0.5 0.5	2.10E-03 2.20E-03 2.30E-03 2.30E-03	9.30E-02 9.50E-02 9.80E-02 9.80E-02	16h DOWN 13 transcripts
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment	9 15 4 4	0.5 0.5	2.10E-03 2.20E-03 2.30E-03 2.30E-03	9.30E-02 9.50E-02 9.80E-02 9.80E-02	16h DOWN 13 transcripts
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment r negative regulation of signal transduction Dependent sets development	9 15 4 4 3	1.2 2 0.5 0.5 6.8 4.5	2.10E-03 2.20E-03 2.30E-03 2.30E-03 2.50E-03	9.30E-02 9.50E-02 9.80E-02 9.80E-02 5.50E-01	16h DOWN 13 transcripts 19h DOWN
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment i negative regulation of signal transduction Peyer's patch development	9 15 4 4 4 3 2	1.2 2 0.5 0.5 6.8 4.5	2.10E-03 2.20E-03 2.30E-03 2.30E-03 2.50E-03 1.10E-02	9.30E-02 9.50E-02 9.80E-02 9.80E-02 5.50E-01 8.20E-01	16h DOWN 13 transcripts 19h DOWN 49 transcripts
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment r negative regulation of signal transduction Peyer's patch development negative regulation of oligodendrocyte differentiation	9 15 4 4 4 3 2 2	1.2 2 0.5 0.5 6.8 4.5 4.5	2.10E-03 2.20E-03 2.30E-03 2.30E-03 2.30E-03 1.10E-02 2.40E-02	9.30E-02 9.50E-02 9.80E-02 9.80E-02 9.80E-02 5.50E-01 8.20E-01 9.20E-01	16h DOWN 13 transcripts 19h DOWN 49 transcripts
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment r negative regulation of signal transduction Peyer's patch development negative regulation of oligodendrocyte differentiation olfactory bulb development	9 15 4 4 3 2 2 2 2 2	1.2 2 0.5 0.5 0.5	2.10E-03 2.20E-03 2.30E-03 2.30E-03 2.30E-03 1.10E-02 2.40E-02 4.10E-02	9.30E-02 9.50E-02 9.80E-02 9.80E-02 5.50E-01 8.20E-01 9.20E-01 9.60E-01	16h DOWN 13 transcripts 19h DOWN 49 transcripts
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment r negative regulation of signal transduction Peyer's patch development negative regulation of oligodendrocyte differentiation olfactory bulb development DNA reolication	9 15 4 4 3 2 2 2 3	1.2 2 0.5 0.5 6.8 4.5 4.5 4.5 6.8	2.10E-03 2.20E-03 2.30E-03 2.30E-03 2.30E-03 1.10E-02 2.40E-02 4.10E-02	9.30E-02 9.50E-02 9.80E-02 9.80E-02 9.80E-02 5.50E-01 8.20E-01 9.20E-01 9.50E-01	16h DOWN 13 transcripts 19h DOWN 49 transcripts
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment i negative regulation of signal transduction Peyer's patch development negative regulation of oligodendrocyte differentiation olfactory bulb development DNA replication regulation of cell proliferation	9 15 4 4 3 2 2 2 3 3	1.2 2 0.5 0.5 6.8 4.5 4.5 6.8 6.8	2:10E-03 2:20E-03 2:30E-03 2:30E-03 2:30E-03 2:50E-03 1:10E-02 2:40E-02 4:60E-02 6:30E-02	9.30E-02 9.50E-02 9.80E-02 9.80E-02 5.50E-01 8.20E-01 9.20E-01 9.50E-01 9.50E-01 9.50E-01	16h DOWN 13 transcripts 19h DOWN 49 transcripts
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment regative regulation of signal transduction Peyer's patch development negative regulation of oligodendrocyte differentiation olfactory bulb development DNA replication PNA replication DNA replication	9 15 4 4 2 2 2 3 3 3 2 2 3 3 3 3 3	1.2 2 0.5 0.5 6.8 4.5 4.5 6.8 6.8 6.8 4.5	2.10E-03 2.20E-03 2.30E-03 2.30E-03 2.30E-03 2.50E-03 1.10E-02 2.40E-02 4.10E-02 4.60E-02 6.30E-02 6.30E-02	9.30E-02 9.50E-02 9.80E-02 9.80E-02 9.80E-02 5.50E-01 8.20E-01 9.20E-01 9.50E-01 9.50E-01 9.70E-01 9.60E-01	16h DOWN 13 transcripts 19h DOWN 49 transcripts
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment	9 15 4 4 2 2 2 3 3 2 2 2 3 3 2 2 2 2 2 2 2 2 3 2	1.2 2 0.5 0.5	2:10E-03 2:20E-03 2:30E-03 2:30E-03 2:30E-03 1:10E-02 2:40E-02 4:10E-02 4:60E-02 6:30E-02 6:80E-02	9.30E-02 9.50E-02 9.80E-02 9.80E-02 9.80E-02 5.50E-01 8.20E-01 9.20E-01 9.60E-01 9.50E-01 9.70E-01 9.60E-01	16h DOWN 13 transcripts 19h DOWN 49 transcripts
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment	9 15 4 4 3 2 2 3 3 2 3 2 3 3 2 3 3 2 6	1.2 2 0.5 0.5 0.5 6.8 4.5 4.5 6.8 6.8 5	2.10E-03 2.20E-03 2.30E-03 2.30E-03 2.30E-03 1.10E-02 2.40E-02 4.10E-02 4.60E-02 6.30E-02 6.80E-02 9.30E-07	9.30E-02 9.50E-02 9.80E-02 9.80E-02 5.50E-01 8.20E-01 9.20E-01 9.50E-01 9.50E-01 9.50E-01 9.50E-01 9.50E-01 9.60E-01 6.40E-04	16h DOWN 13 transcripts 19h DOWN 49 transcripts 22h DOWN
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment No GO Term enrichment	9 15 4 4 3 2 2 2 2 3 3 2 6 8	1.2 2 0.5 0.5 0.5 4.5 4.5 4.5 6.8 4.5 5 6.6	2.10E-03 2.20E-03 2.30E-03 2.30E-03 2.30E-03 2.50E-03 1.10E-02 2.40E-02 4.10E-02 4.10E-02 6.30E-02 6.80E-02 9.30E-07 1.80E-06	9.30E-02 9.50E-02 9.80E-02 9.80E-02 9.80E-02 5.50E-01 8.20E-01 9.20E-01 9.50E-01 9.50E-01 9.50E-01 9.60E-01 6.40E-04 6.10E-04	16h DOWN 13 transcripts 19h DOWN 49 transcripts 22h DOWN 138 transcripts
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment regative regulation of signal transduction Peyer's patch development negative regulation of oligodendrocyte differentiation olfactory bulb development DNA replication PNA replication initiation f DNA replication initiation G1/S transition of mitotic cell cycle DNA replication of mitotic cell cycle DNA replication of mitotic cell cycle DNA replication of mitotic cell cycle	9 15 4 4 2 2 2 2 3 2 2 3 3 6 8 9	1.2 2 0.5 0.5 0.5 0.5 6.8 4.5 4.5 6.8 6.8 4.5 5 6.6 6.6 6.6	2.10E-03 2.20E-03 2.30E-03 2.30E-03 2.30E-03 1.10E-02 2.40E-02 4.10E-02 4.60E-02 6.30E-02 9.30E-07 1.80E-06	9.30E-02 9.50E-02 9.80E-02 9.80E-02 9.80E-02 9.80E-01 9.20E-01 9.20E-01 9.50E-01 9.50E-01 9.50E-01 9.50E-01 9.50E-01 9.60E-01 6.40E-04 6.40E-04 6.40E-02	16h DOWN 13 transcripts 19h DOWN 49 transcripts 22h DOWN 138 transcripts
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type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment No GO Term enrichment	9 15 4 4 3 2 2 2 3 2 2 3 2 3 2 6 8 8 4	1.2 2 0.5 0.5 0.5 0.5 6.8 4.5 4.5 6.8 4.5 5 6.6 6.6 3.3 3	2.10E-03 2.20E-03 2.30E-03 2.30E-03 2.30E-03 2.30E-03 1.10E-02 2.40E-02 4.10E-02 4.10E-02 4.10E-02 6.30E-02 6.30E-02 9.30E-07 1.80E-06 2.80E-05 5.80E-04	9.30E-02 9.50E-02 9.80E-02 9.80E-02 9.80E-02 5.50E-01 8.20E-01 9.20E-01 9.20E-01 9.60E-01 9.60E-01 9.60E-01 6.40E-04 6.40E-03 9.40E-02	16h DOWN 13 transcripts 19h DOWN 49 transcripts 22h DOWN 138 transcripts
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type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment No GO Term enrichment	9 15 4 4 3 2 2 2 3 2 2 3 2 6 8 4 3 4	1.2 2 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 6.8 4.5 6.8 6.8 4.5 5 6.6 6.6 3.3 2.5 2.5 2.5	2.10E-03 2.20E-03 2.30E-03 2.30E-03 2.30E-03 2.30E-03 1.10E-02 2.40E-02 4.10E-02 4.60E-02 6.30E-02 6.30E-02 9.30E-07 1.80E-06 2.80E-02 9.30E-07 1.80E-06 2.80E-02 5.80E-04 1.70E-03 2.70E-42	9.30E-02 9.50E-02 9.80E-02 9.80E-02 9.80E-02 9.80E-02 9.20E-01 9.20E-01 9.20E-01 9.20E-01 9.20E-01 9.50E-01 9.70E-01 9.60E-01 6.40E-03 9.40E-02 2.10E-01 2.40E-45	16h DOWN 13 transcripts 19h DOWN 49 transcripts 22h DOWN 138 transcripts
type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment r negative regulation of signal transduction Peyer's patch development negative regulation of oligodendrocyte differentiation olfactory bulb development DNA replication DNA replication initiation f DNA replication initiation f DNA replication of mitotic cell cycle DNA replication negative regulation of Notch signaling pathway negative regulation of oligodendrocyte differentiation	9 15 4 4 3 2 2 2 3 2 3 2 3 2 3 2 6 8 4 3 2 3	1.2 2 0.5 0.5 0.5 0.5 6.8 4.5 4.5 6.8 6.8 4.5 5 6.6 3.3 2.5 8.8	2.10E-03 2.20E-03 2.30E-03 2.30E-03 2.30E-03 1.10E-02 2.40E-02 4.10E-02 4.60E-02 6.30E-02 6.30E-02 9.30E-07 1.80E-06 2.80E-05 5.80E-04 1.70E-03 2.70E-18	9.30E-02 9.50E-02 9.80E-02 9.80E-02 9.80E-02 9.80E-02 9.20E-01 9.20E-01 9.50E-01 9.40E-02 2.10E-01 2.40E-15 	16h DOWN 13 transcripts 19h DOWN 49 transcripts 22h DOWN 138 transcripts 24h DOWN
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type I interferon signaling pathway positive regulation of I-kappaB kinase/NF-kappaB signaling regulation of chromosome segregation mitotic spindle midzone assembly No GO Term enrichment	9 15 4 4 2 2 2 2 2 3 2 2 3 2 3 2 3 3 2 3 3 13 20 17 7	1.2 2 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 6.8 4.5 6.8 6.8 4.5 5 6.6 3.3 2.5 8.8 13.6 11.6 4.8	2.10E-03 2.20E-03 2.30E-03 2.30E-03 2.30E-03 2.30E-03 1.10E-02 2.40E-02 4.10E-02 4.60E-02 6.30E-02 6.30E-02 9.30E-07 1.80E-06 2.80E-05 5.80E-04 1.70E-03 2.70E-18 2.90E-17 1.20E-08	9.30E-02 9.50E-02 9.80E-02 9.80E-02 9.80E-02 9.80E-02 9.20E-01 9.20E-01 9.20E-01 9.50E-01 9.50E-01 9.50E-01 9.50E-01 9.60E-01 9.60E-01 9.60E-01 9.40E-02 2.10E-01 2.40E-15 1.30E-15 2.70E-06	16h DOWN 13 transcripts 19h DOWN 49 transcripts 22h DOWN 138 transcripts 24h DOWN 166 transcripts
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 Table S3: Correlation analysis between the BrdU-Seq and Chr-RNA-Seq time points and repeats. Related to Figure 1.

	14h	16h	19h	22h	24h
14h	1	0.991	0.99	0.978	0.974
16h		1	0.988	0.96	0.959
19h			1	0.988	0.988
22h				1	0.998
24h					1

Correlation between timepoints based on RPM for each gene > 1RPM

14h = G1/S 16h = Early S 19h = Early/Mid S 22h = Mid S 24h = Mid/Late S28h = Late S/G2

Correlations between biological repeats based on RPM for each gene >1 RPM

	V			<u> </u>	
	14h	16h	19h	22h	24h
14h	0.987				
16h		0.992			
19h			0.992		
22h				0.996	
24h					0.994

Table S4: Gene ontology analysis of G-MiDS hotspot transcripts, using the online DAVID Bioinformatic Resources (https://david.ncifcrf.gov). Related to Figure 7.

GO Term	Counts	p-Value	Benjamini
transcription, DNA-templated/	75/	1.30E-06/	1.90E-03/
regulation of transcription, DNA-templated/	62/	1.50E-06/	1.10E-03/
synaptic transmission, glutamatergic/	5/	9.90E-04/	4.00E-01/
positive regulation of protein phosphorylation/	9/	6.70E-03/	9.30E-01/
endocytic recycling/	4/	1.50E-02/	9.90E-01/
fatty acid beta-oxidation/	5/	1.50E-02/	9.80E-01/
positive regulation of transcription, DNA-templated/	20/	1.80E-02/	9.80E-01/
protein targeting to plasma membrane/	4/	1.80E-02/	9.70E-01/
peptidyl-tyrosine phosphorylation/	9/	1.90E-02/	9.60E-01/
regulation of defence response to virus by virus/	4/	2.20E-02/	9.70E-01/
positive regulation of GTPase activity/	21/	2.30E-02/	9.60E-01/
ER to Golgi vesicle-mediated transport/	9/	2.40E-02/	9.60E-01/
regulation of small GTPase mediated signal transduction/	8/	2.80E-02/	9.60E-01/
cell migration/	9/	3.50E-02/	9.80E-01/
positive regulation of protein kinase B signalling/	6/	3.60E-02/	9.80E-01/