SUPPLEMENTARY METHODS

Microarray analysis supporting data in Fig. 2, Fig. 3, and Fig. S1. We produce a normalized, smoothed signal or $\log_2$ ratio of treatment (origin libraries) over control (genomic DNA) as a function of the genomic coordinate in the following way. We first apply the quantile normalization procedure to replicate arrays, which essentially ensures that the intensity distributions are the same. Treatment and control array intensities are then scaled so that their median value across the array is the same. We then apply a smoothing procedure whereby we calculate a median-like value (i.e., Hodges-Lehmann estimator) for the $\log_2$ ratios of treatment over control probes that fall within a 1 kb window that we slide across ENCODE regions. More specifically, after normalization, the two-sample Wilcoxon Rank Sum test was then applied to all replicate $\log_2$(max(PM-MM,1) treatment and control values that fell within a 1 kb sliding window (Cawley et al. 2004) to arrive at a Hodges-Lehmann estimator (Hollander and Wolf 1999) of the $\log_2$ ratios of cloned origin fragments over genomic control DNA (i.e., signal) for every probe position on the array. We chose a window size of 1 kb, which is ~three-fold smaller than the typical EcoRI fragment in the ENCODE regions (median and mean lengths are 2,645 bp and 3,851 bp, respectively) and considerably smaller than the average trapped fragment (~6.5 kb). This relatively modest window size minimizes the smoothing of probe intensities across two adjacent EcoRI fragments, but encompasses up to ~45 probes within the window for estimating enrichments over control DNA. We then calculated the median of the Hodges-Lehmann estimator of the $\log_2$ ratio of origin library over control DNA within every EcoRI fragment to arrive at the medRI values. We applied a medRI cutoff of 0.2 (see Fig. S1 and S2) and required that at least eight positive probes (i.e., signal greater than 0) for an EcoRI fragment be called positive (bubble-containing).

Calculation of the False Discovery Rate (supporting values in the main text and Figure S1C). We estimated the False Discovery Rate (FDR) corresponding to the $\log_2$ medRI cutoff value of 0.2 for early-HeLa, log-HeLa, and log-GM06990. We randomly permuted the signals of the probes, recalculated the medRI value for the randomized data, and applied a 0.2 cutoff to estimate the number of false positives. This calculation was performed 100 times and generated the distribution of false positives shown in Figure S1C. The FDR was estimated by calculating the mean number of false positives from

the 100 random permutations of probe-signal data and dividing by the number of actual positive calls for early-HeLa, log-HeLa, and log-GM06990. We found 2.27, 4.25, and 14.74 mean false positives for early S-phase HeLa, log-phase HeLa, and log-phase GM06990, which correspond to FDRs of 0.4%, 0.6% and 1.5%, respectively.

Complete and Restricted Null Models. We used random permutation models to assess the statistical significance of origin clustering, as well as the association between origin fragments and functional elements, including transcribed genes and histone marks. With cluster analysis, *all* of the EcoRI fragments (isolated and zonal as well as non-bubble-containing) were randomly permuted or shuffled 10,000 times within each ENCODE region. This procedure generated 10,000 instances of randomly permuted EcoRI fragments. We note that this random permutation procedure separated zonal fragments and mixed them together with origin-negative, isolated, and zonal fragments from other zones. However, this approach preserves the number and genomic coverage of bubble-containing fragments within each ENCODE region. We refer to this as the *complete* null model, which allows an assessment of the significance of associations between genes and distinct fragment classes within any given zone category (as in Table IB-E).

However, as discussed, the number of zones and the average number of fragments within zones are over-represented in the experimental or actual data relative to the complete null data, which could lead to over-estimates of the significance of associations between zones, their fragments, and active genes. Therefore, a *restricted* null model also was generated in which isolated fragments, origin-negative fragments, and *zones treated as units* were randomly permuted 10,000 times within their ENCODE regions (Table IF&G). This procedure generated 10,000 instances of randomly permuted zones and EcoRI fragments. Thus, zonal fragments are kept together and not separated in the restricted null model. As in the complete null model, the number and genomic coverage of the bubble-containing fragments is preserved within every ENCODE region. This allowed us to assess the significance of the association between zones and active genes, keeping the number and size of zones the same in the restricted random data and the actual data.

Cluster analysis supporting Fig. 4 and Table SII. Two or more adjacent bubble-containing EcoRI fragments were classified as a cluster or zone. All other bubble-containing fragments were classified as isolated. Because each bubble-containing EcoRI fragment contains at least one initiation site, two or more contiguous bubble-containing EcoRI fragments indicate independent, neighboring origin firing events, which we define as a cluster or zone of initiation. Using the random permutation null model, we find that the number of zones, the mean number of fragments in zones, and the total number of fragments in zones are highly significant (Table SII).

Origin-gene interaction analysis supporting Fig. 5 and Table 1. We used RefSeq annotations (Pruitt et al. 2007) to compare origin activity and gene sequences. We also used Affymetrix transcriptome data to determine which genes were expressed in log-phase HeLa and GM06990 cells. Specifically, the sites of transcription were down-loaded and overlapped with RefSeq exons. When the fraction of each RefSeq gene that overlapped the sites of transcription was calculated, a bimodal distribution of unexpressed and expressed genes was observed, with a dip near 0.5. Thus, for a gene to be classified as transcribed, we required that 60% or more of a RefSeq gene's UTRs and exons overlap sites of transcription.

For the purpose of significance testing, origin fragments or zones treated as units that *completely overlapped* transcribed regions of the genome (class or category 1; Fig. 5A) were classified as transcribed. Origin fragments or zones treated as units that completely or partially overlapped *non-transcribed regions* (classes or categories 5-9; Fig. 5A) were classified simply as non-transcribed.

An important question in the replication field is whether transcription and origin firing can occur on the same DNA template simultaneously. Given that a large number of bubble-containing fragments *partially* overlap transcribed loci, we arrived at a classification scheme that assessed the likelihood that an origin could have fired in a transcribed region of the fragment. Thus, we took into account whether a fragment contained a transcription-free region large enough to accommodate an origin recognition complex (ORC). Additionally, the trapping method likely captured only those bubble-containing fragments in which the start site was beyond a certain distance from the edges of the EcoRI fragment.

Thus, we arrived at a minimum distance from the edge of EcoRI fragments in which an origin could have fired and been detected, and included this distance in our classification procedure as detailed below.

Origin fragments or zones treated as units that *partially overlapped* transcribed regions (classes or categories 2, 3, and 4; Fig. 5A) are necessarily ambiguous. Therefore, they were designated as transcribed, not transcribed, or indeterminate in the following way: each fragment was divided into *segments* with different transcription states. For assessing possible concurrence of initiation of replication and transcription, we assumed a liberal 500 bp footprint by the origin recognition complex *in vivo* (ORC; Diffley and Cocker 1992). Also, since we found few bubble-containing fragments below ~200 bp, we assumed that origins had to fire > 100 bp from the edges of the EcoRI fragment in order to be trapped and therefore *detectable*. Of course, the entire 500 bp ORC footprint does not have to be completely contained within the fragment.

If an origin could have fired in a detectable region of the fragment or zone that was transcribed ($\geq$ 1 bp overlap), then we labeled that segment of the fragment or zone as transcribed (T). If an origin could have fired in a detectable region that was free of transcription, that segment was annotated as not transcribed (NT), provided that there was a 500 bp transcription-free window that overlapped the detectable regions of the bubble-containing fragment or zone. If a fragment or zone contained T but no NT segments, then it was classified as transcribed. If a fragment or zone contained NT and no T segments, it was classified as not transcribed. If a fragment or zone contained both T and NT segments, then it was classified as indeterminate. As an example, if a bubble fragment completely contains a transcribed gene near its center, and there is a $\geq$ 500 bp transcription-free region upstream or downstream, it was classified as indeterminant.

When assessing the fraction of RefSeq genes that overlapped origins, we represented overlapping genes (including alternative isoforms) by the group's minimum and maximum coordinates. If a gene within the group of overlapping genes was classified as active, then the group was classified as active.

Histone marks unique to origins (supporting discussion in main text and Table SIV). We assessed the significance of the association between bubble-containing fragments and each activating histone mark that was mapped to ENCODE regions in HeLa and GM06990 by performing chi-squared

tests of independence. Specifically, we built 2x2 contingency tables of counts of EcoRI fragments that were and were not bubble-containing (rows) and whose center was or was not within 7.5 kb of a given active histone mark (columns). We calculated the chi-squared statistic and associated p-values using the statistical software environment R (http://www.r-project.org/).

To distinguish the association of histone marks and origin activity from histone marks near or in promoters, isolated fragments and zones were categorized into ten mutually exclusive classes. Isolated fragments or zones that overlap transcribed or non-transcribed genes with (Hp^*) or without (Hp^o) an activating histone mark within ±2 kb of the transcription start site were put into categories 1-4. Isolated fragments or zones that *did not overlap* a gene were placed in the remaining six categories. If the center of an isolated fragment or a zonal end-fragment was within 7.5 kb of the 5' or 3' end of a gene, the isolated fragment or zone was placed in one of categories 5-8. If an activating histone mark was within 7.5 kb from a category 5-8 isolated fragment center or zonal end-fragment center, the isolated fragment or zone was put into category 5 (5' – H*) or 7 (3' – H*); if an activating histone mark was *not within 7.5 kb* of a category 5-8 isolated fragment or zonal end-fragment center, the isolated fragment or zone was put into category 6 (5' - H^o) or 8 (3' - H^o). Isolated fragments or zonal end-fragments whose centers were >7.5 kb from a gene were classified as intergenic. Intergenic isolated fragments or zonal end-fragments whose centers were within 7.5 kb of an activating histone mark were put into category 9 (intergenic – H*); otherwise, they were put into category 10 (intergenic - H^o).

Given the strong association between origins/zones and transcribed genes, we further assessed the extent to which origin activity within genes was associated with activating histone marks that were not located within the promoters themselves. Thus, isolated origin fragments or zones that overlapped genes were also placed in categories 11-14. If the center of a genic fragment or zonal end-fragment was not within 7.5 kb of an activating histone mark, the fragment or zone was put into category 11 (in-gene - H^o). Genic histone-associated isolated fragments or zones that were within genes that either did not or did contain an activating histone mark within ±2 kb of that gene's transcription start site were placed in categories 12 (in-gene – H* but no Hp^*) and 13 (in-gene – H* and Hp^*), respectively. Finally, genic histone-associated isolated fragments or zones that were within non-transcribed genes were put into

category 14 (in-gene – H* & non-Tx). For simplicity, we annotated zones as units and did not annotate their fragments separately. Graphic representations of the fourteen annotation classes discussed above are available from J.L.H. upon request (jlh2d@virginia.edu).

We again assessed the significance of the overlaps/associations of isolated fragments and zones with the 14 annotation classes listed above using our complete (data not shown) and restricted null random models. Based on both models, zones were significantly associated with transcribed genes that contained activating marks in their promoters (75 zones) and those that did not (5 zones) in HeLa cells, while in GM06990 cells, only the overlap with transcribed genes that contained activating marks in their promoters was significant (55 zones). In HeLa cells, there was significant over-representation of isolated fragments with genic loci that contain an activating mark in the promoter of either transcribed genes (p-value $< 10^{-4}$) or silent genes (p-value=0.0065), based on the restricted null model only. Interestingly, the intergenic regions in HeLa and GM06990 cells contained 830 and 1,040 activating mark loci, yet zones were not significantly associated with these. In GM06990 cells, there is a mildly significant association between isolated fragments and activating marks located in intergenic regions based on the restricted null model (p-value 0.034). These results suggest that origins, and zones in particular, are strongly associated with activating chromatin marks at the 5' ends of transcribed genes, but are not overrepresented near activating marks outside of promoters.

SUPPLEMENTARY REFERENCE

Hollander, M., and Wolf, D.A. (1999). Nonparametric Statistical Methods (2nd Edition, John Wiley and Sons).

SUPPLEMENTARY TABLE LEGENDS

Table SI. Mean size and signal strength of overlapping & non-overlapping fragment signals in microarray comparisons. A. Comparison between signals from two different early S-phase HeLa hybridization replicates. B. Comparison between signals from two log-phase HeLa biological replicates. C. Comparison between signals from early S-phase and log-phase HeLa libraries. D. Comparision between signals from log-phase HeLa and log-phase GM06990 libraries. The column labeled *# Signals* is the number of medRI signals above the 0.2 cutoff in the ENCODE regions. *Sample percentages* are

calculated by dividing the number of overlapping fragments by the number of positive fragments in that sample. *mean size* refers to mean bubble-containing fragment size, while *mean strength* refers to the mean signal strength of bubble-containing fragments.

Table SII. Significance of fragment clustering. Assessment of the significance of the clustering of bubble-containing fragments into zones for early-HeLa, log-HeLa and log-GM06990. A cluster or zone is defined as two or more contiguous bubble-containing fragments that pass the 0.2 medRI cutoff. Statistics were calculated using the complete null model in which EcoRI fragments were randomly permuted within each ENCODE region 10,000 times. P-values were calculated by comparing the number of experimentally observed or actual # of clusters to those found in the random data; # actual is the number of experimentally observed clusters in the data, fold-change is the # actual divided by the mean random number of clusters; mean random is calculated by taking the mean of the number of clusters found in the 10,000 random permutations of EcoRI fragments; sd random is the standard deviation of the number of clusters found in the 10,000 random permutations of EcoRI fragments; and z is the z-score [(# actual - mean random)/(sd random)], which is the number of standard deviations of the random data that divide the # actual and mean random values.

Table SIII. Significance of origin-gene interactions. Assessment of the significance of the overlap between transcribed (tx), non-transcribed (non-tx) genes, intergenic loci, and isolated and zonal bubble-containing fragments for log-HeLa and log-GM06990. Isolated fragments, zones, and fragments within zones were classified according to the definitions shown within panel A1 of Table I and Fig. 5B2. For sub-tables A1-B2, statistics were calculated using the complete null model in which EcoRI fragments were randomly permuted within each ENCODE region 10,000 times. For sub-tables C1 and C2, statistics were calculated using the restricted null model in which EcoRI fragments, isolated bubble-containing fragments, and zones treated as units were randomly permuted within each ENCODE region 10,000 times. P-values were calculated by comparing the number of experimentally observed or actual # of clusters to those found in the random data; # actual is the number of experimentally observed clusters in the data; fold-change is the # actual divided by the mean random number of clusters; mean random is calculated by taking the mean of the number of clusters found in the 10,000 random permutations of

EcoRI fragments; sd random is the standard deviation of the number of clusters found in the 10,000 random permutations of EcoRI fragments; and z is the z-score [(# actual - mean random)/(sd random)], which is the number of standard deviations of the random data that divide the # actual and mean random values.

Table SIV. Isolated & Zones – Randomization for histone marks. Assessment of the significance of the overlap between activating histone marks, transcribed (tx) genes, non-transcribed (non-tx) genes, intergenic loci and isolated and zonal bubble-containing fragments for log-HeLa and log-GM06990. Below, we provide a key that specifies the meaning of the 14 annotation categories involving activating histone marks, transcribed (tx) genes, non-transcribed (non-tx) genes, and intergenic loci. Statistics were calculated using the complete null model where EcoRI fragments were randomly permuted within each ENCODE region 10,000 times. P-values were calculated by comparing the number of experimentally observed or actual # of clusters to those found in the random data; # actual is the number of experimentally observed clusters in the data; fold-change is the # actual divided by the mean random number of clusters; mean random is calculated by taking the mean of the number of clusters found in the 10,000 random permutations of EcoRI fragments; sd random is the standard deviation of the number of clusters found in the 10,000 random permutations of EcoRI fragments; and z is the z-score [(# actual - mean random)/(sd random)], which is the number of standard deviations of the random data that divide the # actual and mean random values.

	Notations used in Table SIV	**Key**
1	+/-2 kb TSS – Hp*/Tx	Fragment (isolated/zone) overlaps a transcribed gene by $\geq$ 1 bp with an activating histone mark within +/-2kb of the TSS
2	+/-2 kb TSS – Hp^{o}/Tx	Fragment (isolated/zone) overlaps a transcribed gene by $\geq$ 1 bp with*out* an activating histone mark within +/-2kb of the TSS
3	+/-2 kb TSS – Hp*/non-Tx	Fragment (isolated/zone) overlaps a non-transcribed gene by $\geq$ 1 bp with an activating histone mark within +/-2kb of the TSS
4	+/-2 kb TSS – Hp^{o}/non-Tx	Fragment (isolated/zone) overlaps a non-transcribed gene by $\geq$ 1 bp with*out* an activating histone mark within +/-2kb of the TSS
5	5' – H*	Center of isolated fragment or zonal end-fragment is within 7.5kb (upstream) of the 5' end of a gene & (an activating histone mark is within 7.5 kb of the isolated fragment center/zonal end fragment centers (or) an activating histone mark overlaps with isolated/zonal fragments by $\geq$ 1 bp)
6	5' – H^{o}	Center of isolated fragment or zonal end-fragment is within 7.5kb (upstream) of the 5' end of a gene & (an activating histone mark is *not* within 7.5 kb of the isolated fragment center/zonal end fragment centers (and) an activating histone mark does *not* overlap with isolated/zonal fragments)
7	3' – H*	Center of isolated fragment or zonal end-fragment is within 7.5kb (downstream) of the 3' end of a gene & (an activating histone mark is within 7.5 kb of the isolated fragment center/zonal end fragment centers (or) an activating histone mark overlaps with isolated/zonal fragments by $\geq$ 1 bp)
8	3' – H^{o}	Center of isolated fragment or zonal end-fragment is within 7.5kb (downstream) of the 3' end of a gene & (an activating histone mark is *not* within 7.5 kb of the isolated fragment center/zonal end fragment centers (and) an activating histone mark does *not* overlap with isolated/zonal fragments)
9	Intergenic – H*	Center of isolated fragment or zonal end-fragment is $\geq$ 7.5kb from a gene & (an activating histone mark is within 7.5 kb of the isolated fragment center/zonal end fragment centers (or) an activating histone mark overlaps with isolated/zonal fragments by $\geq$ 1 bp)
10	Intergenic – H^{o}	Center of isolated fragment or zonal end-fragment is $\geq$ 7.5kb from a gene & (an activating histone mark is *not* within 7.5 kb of the isolated fragment center/zonal end fragment centers (and) an activating histone mark does *not* overlap isolated/zonal fragments)
11	In gene - H^{o}	Fragment (isolated/zone) overlaps a gene by $\geq$ 1 bp & (an activating histone mark is *not* within 7.5 kb of the isolated fragment center/zonal end fragment centers (and) an activating histone mark does *not* overlap with isolated/zonal fragments)
12	In gene – H^{*} but no Hp*	Fragment (isolated/zone) overlaps a gene by $\geq$ 1 bp & (an activating histone mark is within 7.5 kb of the isolated fragment center/zonal end fragment centers (or) an activating histone mark overlaps with isolated/zonal fragments by $\geq$ 1 bp) and the isolated fragment/zone does *not* contain an activating histone mark within +/-2kb of that gene's TSS
13	In gene – H^{*} and Hp*	Fragment (isolated/zone) overlaps a gene by $\geq$ 1 bp & (an activating histone mark is within 7.5 kb of the isolated fragment center/zonal end fragment centers (or) an activating histone mark overlaps with isolated/zonal fragments by $\geq$ 1 bp) and the isolated fragment/zone contains an activating histone mark within +/-2kb of the TSS
14	In gene – H^{*} & non-Tx	Fragment (isolated/zone) overlaps a *non*-transcribed gene by $\geq$ 1 bp & (an activating histone mark is within 7.5 kb of the isolated fragment center/zonal end fragment centers (or) activating histone mark overlaps isolated/zonal fragments by $\geq$ 1 bp)

Table SV. Locations of the ten overlaps among Study 1 (Prioleau) and Study 2 (Dutta) HeLa nascent strand (NS) calls and bubble-containing fragment signals. The locations of the bubble-containing fragments are indicated under the *Signal* column, and their positions relative to local genes (Refseqs) are tabulated under *Genes*. As shown under the *Remarks* column, only two of the ten are completely intergenic; the remaining eight overlap one or more genes, six of which are transcribed.

SUPPLEMENTARY FIGURE LEGENDS

Figure S1. MedRI distributions, qq plots, and false discovery rates (supporting Fig. 2&3). Panel A. Distribution plots (i.e., density or normalized counts on the y-axis) of all medRI values (x-axis) from early-S-phase HeLa, log-phase Hela, and log-phase GM06990 data. All of these plots display a near normal noise distribution about the mode, which is negative in all cases. Panel B. Quantile-quantile plots of the medRI quantiles (y-axis) compared to that of a standard normal distribution (x-axis) from early-S-phase HeLa, log-phase HeLa, and log-phase GM06990 data. These plots confirm a normal noise core in the medRI distributions, with a sharp departure and heavy right signal tail starting at small positive medRI values. Panel C. Distribution plots (i.e., density or normalized counts on the y-axis) of the number of false positives (x-axis) derived by randomly permuting array probe signals, recalculating medRI values, and applying a 0.2 cutoff.

Figure S2. Probe signal values in EcoRI fragments that just pass the 0.2 medRI cutoff. Integrated Genome Browser screen shots of EcoRI fragments whose medRI value is slightly above the 0.2 cutoff. EcoRI fragment boundaries are shown in green and the probe signals are shown in blue. We selected isolated bubble-containing fragments to highlight the fact that positive signal values tend to persist along the central bubble-containing fragment, while the signal values are near zero or negative in the flanking EcoRI fragments. Thus, the positive signal in the bubble-containing fragment and the corresponding positive call are not the result of smoothing positive signal from neighboring EcoRI fragments. Rather, the signal distribution is precisely what would be expected of relatively low copy number cloned bubble-containing fragments that hybridized to the arrays.

Figure S3. Correlations between hybridization or biological replicates are good, while early-S-phase/log-phase and HeLa/GM06990 comparisons are not (supporting Fig. 3). Scatter plots of the following data sets: A) two independent hybridizations with the early-S-phase HeLa origin library; B) the two log-phase HeLa biological replicates; C) early-S-phase- versus log-phase HeLa libraries; and D) log-phase HeLa versus log-phase GM06990 libraries. Pearson correlation coefficients are shown in each panel.

Figure S4. Distance distributions between origin-mark centers (supporting discussion of origin distributions vis-à-vis selected histone marks). Panels A and B. Distribution plots of distances between the center of bubble-containing fragments and activating histone mark sites in log-phase HeLa and GM06990 cells. For reference, also plotted are the center-to-edge distances of bubble-containing fragments. Note that a relatively large percentage of the activating marks overlap bubble-containing fragments and that these distance distributions begin to fall off their peak values at ~7.5kb, which is the distance cutoff used for associating a bubble-containing fragment to an activating histone mark. Panel C. Distribution plots of distances between the center of bubble-containing fragments and repressive histone marks. Here, the distances are much greater than the characteristic half-size of the bubble-containing fragments, indicating that repressive marks tend to be distant from origins.

Figure S1

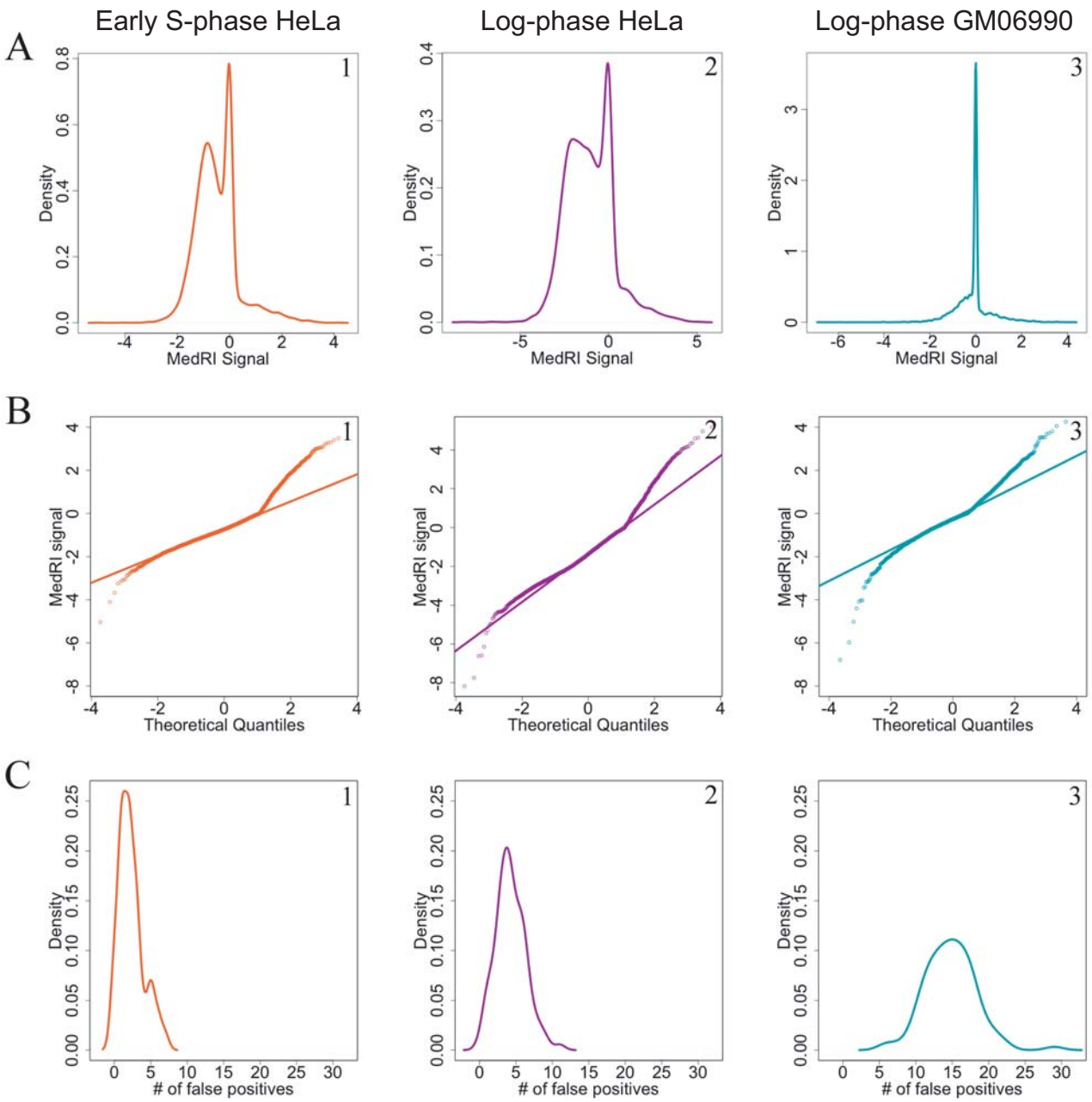
Early S-phase HeLa
Log-phase HeLa
Log-phase GM06990
A
B
C
1
2
3
Density
MedRI Signal
MedRI signal
Theoretical Quantiles
# of false positives

Figure S2

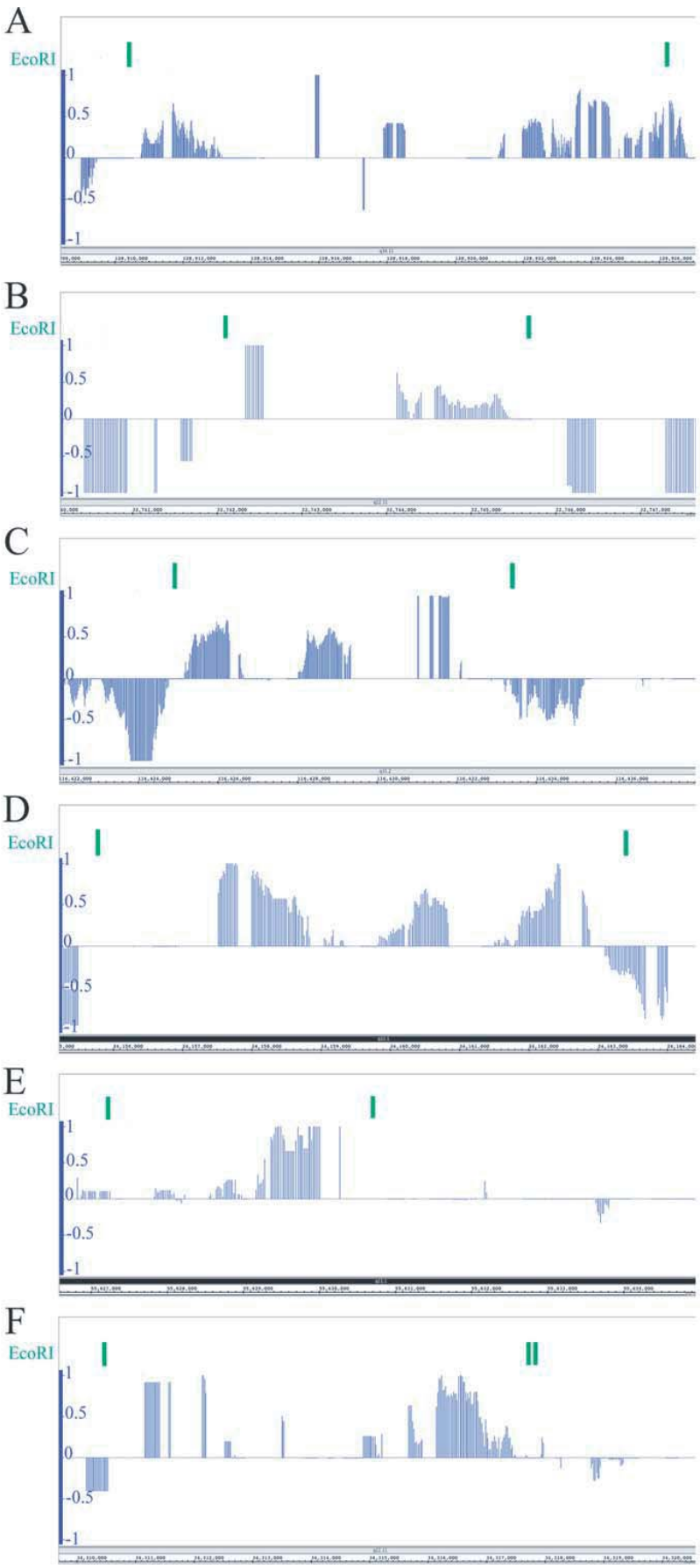
A
EcoRI
1
0.5
0
-0.5
-1
B
EcoRI
1
0.5
0
-0.5
-1
C
EcoRI
1
0.5
0
-0.5
-1
D
EcoRI
1
0.5
0
-0.5
-1
E
EcoRI
1
0.5
0
-0.5
-1
F
EcoRI
1
0.5
0
-0.5
-1

Figure S3

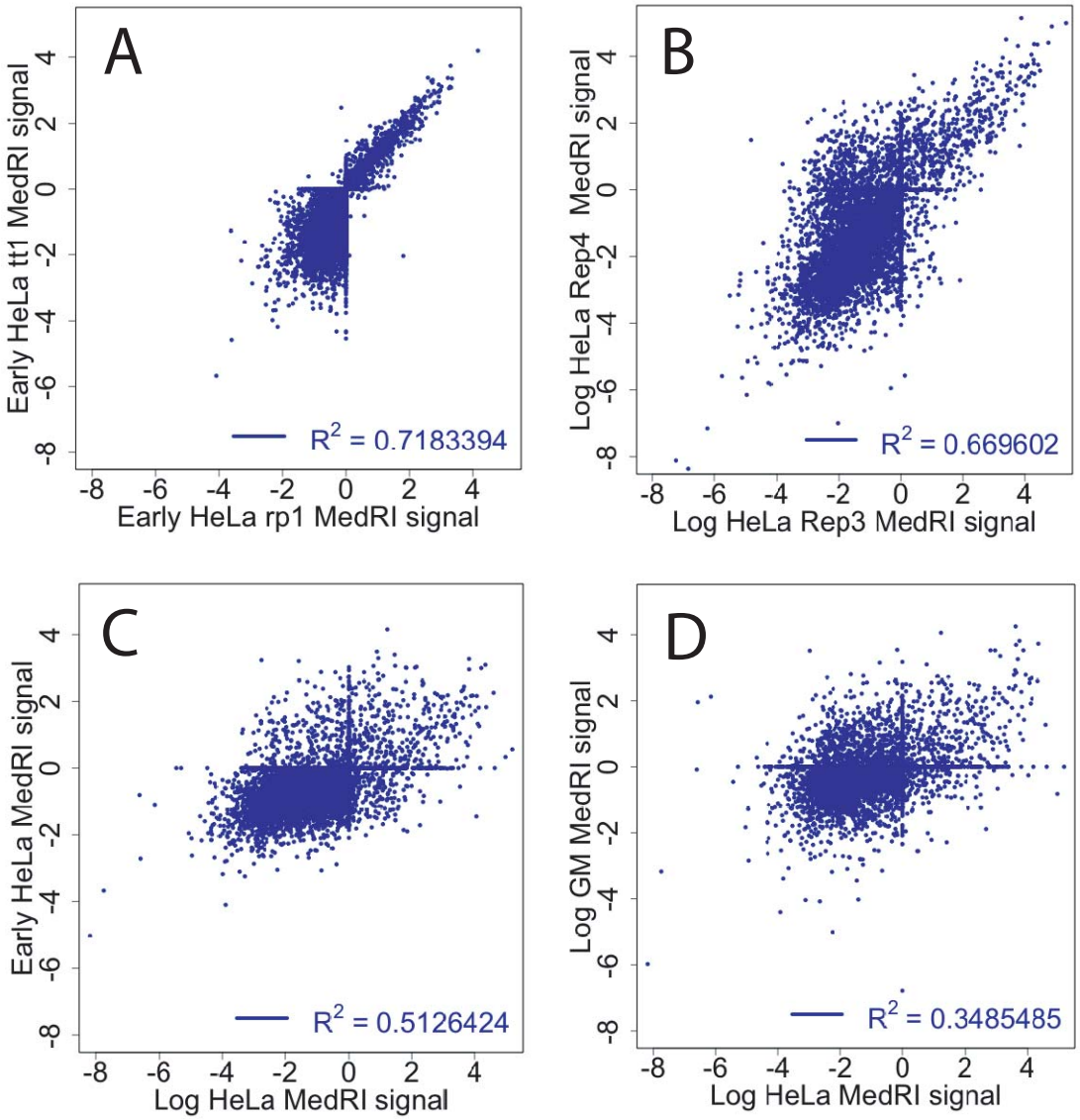
A
Early HeLa tt1 MedRI signal
Early HeLa rp1 MedRI signal
R2 = 0.7183394
B
Log HeLa Rep4 MedRI signal
Log HeLa Rep3 MedRI signal
R2 = 0.669602
C
Early HeLa MedRI signal
Log HeLa MedRI signal
R2 = 0.5126424
D
Log GM MedRI signal
Log HeLa MedRI signal
R2 = 0.3485485

Figure S4

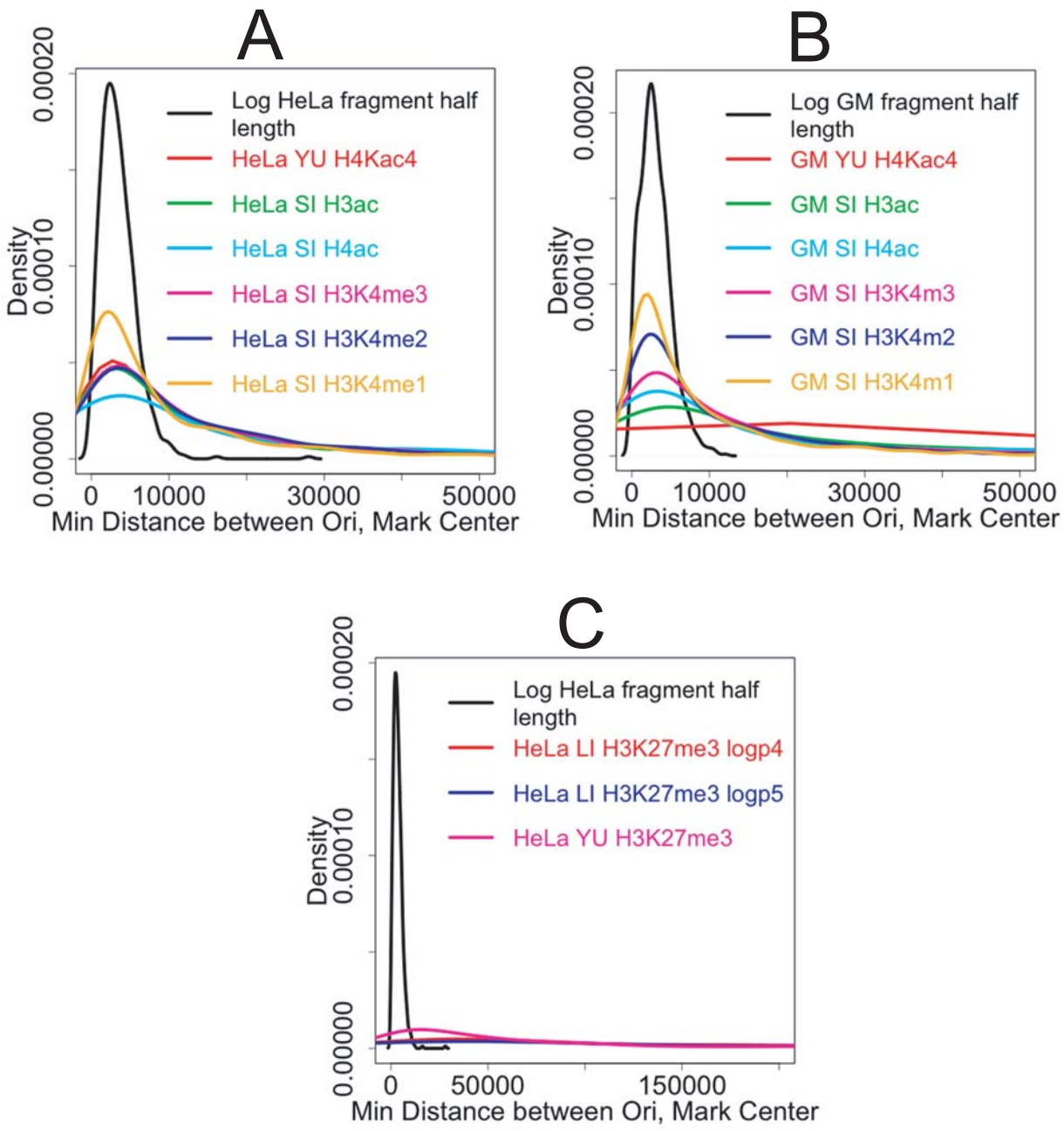
A
Log HeLa fragment half length
HeLa YU H4Kac4
HeLa SI H3ac
HeLa SI H4ac
HeLa SI H3K4me3
HeLa SI H3K4me2
HeLa SI H3K4me1
Density
0.00020
0.00010
0.00000
0
10000
30000
50000
Min Distance between Ori, Mark Center
B
Log GM fragment half length
GM YU H4Kac4
GM SI H3ac
GM SI H4ac
GM SI H3K4m3
GM SI H3K4m2
GM SI H3K4m1
Density
0.00020
0.00010
0.00000
0
10000
30000
50000
Min Distance between Ori, Mark Center
C
Log HeLa fragment half length
HeLa LI H3K27me3 logp4
HeLa LI H3K27me3 logp5
HeLa YU H3K27me3
Density
0.00020
0.00010
0.00000
0
50000
150000
Min Distance between Ori, Mark Center

Table SI – Size/strength of overlapping & non-overlapping fragments

A. Early-S-phase HeLa Rp1 and Tt1

	# Signals	% Rp1	% Tt1	Mean size	Mean strength
Rp1 frags	626				
Tt1 frags	670				
Overlaps	563	89.9%	84.0%	6697	1.294
Unique to Rp1	63			4883	0.540
Unique Tt1	107			5569	0.443
Non-overlapping means				5315	0.479

B. Log HeLa Rep3 and Rep4

	# Signals	% Rep3	% Rep4	Mean size	Mean strength
Rep3 frags	594				
Rep4 frags	1068				
Overlaps	458	77.1%	42.9%	6981	1.788
Unique Rep3	136			5560	0.747
Unique to Rep4	610			6049	0.963
Non-overlapping means				5960	0.924

C. Early-S-phase and Log-phase HeLa

	# Signals	% Early	% Log	Mean size	Mean strength
Early frags	646				
Log frags	657				
Overlaps	282	42.9%	43.7%	7781	1.577
Unique Early-S	364			6335	1.200
Unique to Log	375			5630	1.057
Non-overlapping means				5988	1.129

D. Log-phase HeLa and Log-phase GM06990

	# Signals	% HeLa	% GM	Mean size	Mean strength
Log HeLa frags	657				
Log GM frags	988				
Overlaps	280	42.6%	28.3%	8041	1.557
Unique to HeLa	377			6150	1.241
Unique to GM	708			5357	0.896
Non-overlapping means				5633	1.016

Table SII – Significance of fragment clustering

Early HeLa	p-value	# actual	fold-change	mean random	sd random	z
# of zones	< 0.0001	111	1.41	78.67	6.19	5.22
Mean length	0.8738	15,195	0.94	16,101	787.50	-1.15
Median length	0.5286	14,589	0.99	14,665	861.83	-0.09
Mean # fragments	0.0003	3.39	1.25	2.70	0.18	3.85
Median # fragments	0.2926	3.00	1.30	2.31	0.45	1.52
# isolated fragments	1.0000	380	0.82	465.35	13.32	-6.41
# zonal fragments	< 0.0001	266	1.47	180.65	13.32	6.41

Log HeLa	p-value	# actual	fold-change	mean random	sd random	z
# of zones	< 0.0001	128	1.46	87.81	6.16	6.52
Mean length	0.0611	18,115	1.08	16,769	854.29	1.58
Median length	0.9192	13,626	0.91	14,933	958.20	-1.36
Mean # fragments	0.0003	3.95	1.46	2.70	0.18	7.06
Median # fragments	0.2293	3.00	1.34	2.25	0.42	1.79
# isolated fragments	1.0000	277	0.64	436.38	13.13	-12.14
# zonal fragments	<0.0001	380	1.72	220.62	13.13	12.14

Log GM06990	p-value	# actual	fold-change	mean random	sd random	z
# of zones	< 0.0001	177	1.28	138.46	7.91	4.87
Mean length	0.7387	14,468	0.98	14,854	608.97	-0.63
Median length	0.4561	13,514	1.01	13,442	663.00	0.11
Mean # fragments	< 0.0001	3.53	1.34	2.64	0.14	6.60
Median # fragments	0.0896	3.00	1.43	2.10	0.29	3.12
# isolated fragments	1.0000	538	0.80	668.82	17.07	-7.67
# zonal fragments	< 0.0001	450	1.41	319.18	17.07	7.67

Table SIII – Significance of origin-gene interactions

A1. Log HeLa (277 isolated)	p-value	# actual	fold-change	mean random	sd random	z
1. Fragment in tx gene	0.0043	60	1.32	45.64	5.02	2.86
2. Tx gene(s) in fragment	0.2477	4	1.55	2.58	1.44	0.99
3. Frag overlaps 5' tx gene(s)	0.1115	12	1.46	8.23	2.63	1.44
4. Frag overlaps 3' tx gene(s)	0.0291	14	1.70	8.24	2.62	2.20
5. Frag in non-tx gene	0.8526	66	0.92	71.92	6.12	-0.97
6. Non-tx gene(s) in frag	0.1127	8	1.62	4.93	2.07	1.48
7. Frag overlaps 5' non-tx gene(s)	0.0830	17	1.42	12.00	3.19	1.57
8. Frag overlaps 3' non-tx gene(s)	0.6731	9	0.91	9.90	2.92	-0.31
9. Intergenic	1.0000	87	0.77	113.57	6.70	-3.97
Total transcribed ori fragments	0.0056	60	1.30	46.11	5.03	2.76
Total free from transcription	1.0000	188	0.89	212.53	5.62	-4.37
Total indeterminate fragments	0.0048	29	1.58	18.36	3.70	2.88
Mixed (2, 3, 4) transcribed oris	1.0000	0	0	0.46	0.67	-0.69
Mixed (class 2, 3, 4) non-tx	0.1914	1	4.73	0.21	0.46	1.73
Mixed (class 2, 3, 4) indeterm	0.0048	29	1.58	18.36	3.70	2.88

A2. Log GM (538 isolated)	p-value	# actual	fold-change	mean random	sd random	z
1. Fragment in tx gene	0.4649	64	1.02	63.04	6.07	0.16
2. Tx gene(s) in fragment	0.9577	1	0.36	2,81	1.52	1.19
3. Frag overlaps 5' tx gene(s)	0.2103	13	1.28	10.18	2.91	0.97
4. Frag overlaps 3' tx gene(s)	0.4073	11	1.11	9.92	2.89	0.37
5. Frag in non-tx gene	0.9974	137	0.87	158.37	8.17	-2.62
6.Non-tx gene(s) in frag	0.6734	6	0.90	6.64	2.34	-0.28
7. Frag overlaps 5' non-tx gene(s)	0.0074	25	1.64	15.27	3.55	2.74
8. Frag overlaps 3' non-tx gene(s)	0.0451	20	1.47	13.75	3.34	1.90
9. Intergenic	0.3944	261	1.01	2.58.11	8.87	0.33
Total transcribed ori fragments	0.4508	65	1.02	63.79	6.09	0.20
Total free from transcription	0.7189	449	0.99	452.34	6.73	-0.50
Total indeterminate fragments	0.3402	24	1.10	21.87	4.07	0.53
Mixed (2, 3, 4) transcribed oris	0.5316	1	1.34	0.75	0.85	0.30
Mixed (class 2, 3, 4) non-tx	1.0000	0	0	0.2958	0.54	-0.55
Mixed (class 2, 3, 4) indeterm	0.3402	24	1.10	21.87	4.07	0.53

B1. Log HeLa (380 zonal frags)	p-value	# actual	fold-change	mean random	sd random	z
# Category 1 zones	0.0058	21	1.69	12.44	3.06	2.80
# Category 2 zones	<0.0001	24	4.32	5.56	1.96	9.40
# Category 3 zones	<0.0001	22	2.92	7.52	2.44	5.93
# Category 4 zones	0.0030	13	2.22	5.87	2.20	3.25
# Category 5 zones	0.6073	17	0.97	17.55	3.63	-0.15
# Category 6 zones	0.1836	8	1.44	5.57	2.17	1.12
# Category 7 zones	0.1387	9	1.50	5.98	2.29	1.32
# Category 8 zones	0.9562	2	0.43	4.70	2.05	-1.31
# Category 9 zones	0.9972	12	0.54	22.39	4.13	-2.52
Category 1 zone - # class 1 frags	0.0007	55	1.96	27.99	7.00	3.86
Category 2 zone - # class 1 frags	<0.0001	28	7.98	3.51	2.38	10.28
Category 2 zone - # class 2 frags	0.1905	13	1.82	7.16	5.24	1.11
Category 2 zone - # class 3 frags	<0.0001	16	8.27	1.93	1.37	10.27
Category 2 zone - # class 4 frags	<0.0001	23	3.61	6.37	4.73	3.52
Category 2 zone - # class 5 frags	0.0502	5	4.19	1.19	1.56	2.44
Category 2 zone - # class 6 frags	<0.0001	5	23.21	0.22	0.47	10.28
Category 2 zone - # class 7 frags	0.0118	3	6.03	0.50	0.69	3.63
Category 2 zone - # class 8 frags	0.0001	4	15.22	0.26	0.51	7.29
Category 2 zone - # class 9 frags	<0.0001	19	5.44	3.49	2.29	6.78
Category 3 zone - # class 1 frags	0.0026	16	2.72	5.89	2.96	3.42
Category 3 zone - # class 3 frags	<0.0001	22	3.73	5.89	2.40	6.71
Category 3 zone - # class 4 frags	0.0836	2	3.99	0.50	0.69	2.16
Category 3 zone - # class 5 frags	0.3376	2	1.55	1.29	1.48	0.48
Category 3 zone - # class 6 frags	0.0180	2	10.03	0.20	0.45	4.01
Category 3 zone - # class 7 frags	0.4961	1	1.49	0.67	0.80	0.41
Category 3 zone - # class 8 frags	1.0000	0	0	0.49	0.69	-0.70
Category 3 zone - # class 9 frags	0.1504	7	1.76	3.97	2.46	1.23
Category 4 zone - # class 1 frags	<0.0001	18	4.57	3.94	2.28	6.18
Category 4 zone - # class 4 frags	0.2006	14	1.67	8.37	4.97	1.13
Category 4 zone - # class 5 frags	0.7619	1	0.45	2.20	1.94	-0.62
Category 4 zone - # class 6 frags	1.0000	0	0	0.21	0.45	-0.47
Category 4 zone - # class 7 frags	0.3569	1	2.29	0.44	0.65	0.86
Category 4 zone - # class 8 frags	0.2279	1	3.89	0.26	0.51	1.47
Category 4 zone - # class 9 frags	0.0569	6	2.39	2.51	1.72	2.03
Category 5 zone - # class 5 frags	0.5273	39	0.99	39.31	8.31	-0.04
Category 6 zone - # class 5 frags	0.2439	4	1.70	2.36	1.96	0.84
Category 6 zone - # class 6 frags	0.0469	6	2.39	2.51	1.66	2.10
Category 6 zone - # class 7 frags	0.2265	4	1.70	2.35	1.67	0.99
Category 6 zone - # class 8 frags	0.8001	1	0.62	1.60	1.26	-0.48
Category 6 zone - # class 9 frags	0.5827	4	0.93	4.31	2.52	-0.12
Category 7 zone - # class 5 frags	0.0435	10	2.16	4.62	2.59	2.08
Category 7 zone - # class 7 frags	0.0746	9	1.81	4.96	2.34	1.72
Category 7 zone - # class 8 frags	1.0000	0	0	0.21	0.47	-0.45
Category 7 zone - # class 9 frags	0.1864	6	1.66	3.62	2.23	1.07
Category 8 zone - # class 5 frags	0.7988	2	0.60	3.34	2.13	-0.63
Category 8 zone - # class 8 frags	0.8617	2	0.54	3.67	2.02	-0.83
Category 8 zone - # class 9 frags	0.6022	3	0.90	3.34	2.19	-0.15
Category 9 zone - # class 9 frags	0.9966	26	0.52	49.54	9.97	-2.36

Mixed (cat 2 /class 2,3,4 – tx	0.0387	2	6.22	0.32	0.56	3.01
Mixed (cat 2 /class 2,3,4 – non-tx	1.0000	0	0	0.06	0.25	- 0.24
Mixed (cat 2 /class 3,4 – indeterm	<0.0001	50	3.32	15.08	9.96	3.51
Mixed (cat 3 /class 3,4 – tx	0.1592	1	5.80	0.17	0.41	2.01
Mixed (cat 3 /class 3,4 – non-tx	1.0000	0	0	0.12	0.34	- 0.34
Mixed (cat 3 /class 3,4 – indeterm	<0.0001	23	3.77	6.10	2.49	6.80
Mixed (cat 4 /class 4 – tx	1.0000	0	0	0.14	0.37	- 0.38
Mixed (cat 4 /class 4 – non-tx	0.0685	1	13.99	0.07	0.27	3.44
Mixed (cat 4 /class 4 – indeterm	0.2712	13	1.59	8.15	4.94	0.98
Total # transcribed oris	<0.0001	120	2.86	41.96	7.45	10.48
Total # non-transcribed	0.0181	174	1.21	143.89	13.44	2.24
Total # indeterminate	<0.0001	86	2.93	29.34	7.63	7.42
# of fragments in category 1 zone	0.0007	55	1.96	27.99	7.00	3.86
# of fragments in category 2 zone	<0.0001	116	4.71	24.63	11.72	7.80
# of fragments in category 3 zone	<0.0001	52	2.75	18.90	6.41	5.16
# of fragments in category 4 zone	0.0013	41	2.29	17.92	7.36	3.14
# of fragments in category 5 zone	0.5273	39	0.99	39.31	8.31	- 0.04
# of fragments in category 6 zone	0.1567	19	1.45	13.13	5.43	1.08
# of fragments in category 7 zone	0.0294	25	1.86	13.42	5.39	2.15
# of fragments in category 8 zone	0.7705	7	0.68	10.35	4.79	- 0.70
# of fragments in category 9 zone	0.9966	26	0.52	49.54	9.97	- 2.36

B2. Log GM (450 zonal frags)	p-value	# Actual	fold-change	mean random	sd random	z
# Category 1 zones	0.5605	12	0.99	12.11	3.17	- 0.04
# Category 2 zones	0.0002	12	2.59	4.64	1.84	4.00
# Category 3 zones	<0.0001	23	3.55	6.48	2.37	6.98
# Category 4 zones	0.0616	9	1.78	5.04	2.12	1.87
# Category 5 zones	0.1323	42	1.17	35.97	4.96	1.22
# Category 6 zones	0.7394	4	0.82	4.90	2.07	- 0.44
# Category 7 zones	0.4621	7	1.10	6.38	2.42	0.26
# Category 8 zones	0.6861	5	0.87	5.71	2.28	-0.31
# Category 9 zones	0.1702	63	1.11	56.84	5.93	1.04
Category 1 zone - # class 1 frags	0.4158	28	1.07	26.25	7.04	0.25
Category 2 zone - # class 1 frags	0.0016	11	3.95	2.78	2.12	3.88
Category 2 zone - # class 2 frags	0.3443	7	1.68	4.16	3.27	0.87
Category 2 zone - # class 3 frags	0.0317	5	2.96	1.69	1.34	2.48
Category 2 zone - # class 4 frags	0.0948	7	2.10	3.34	2.37	1.54
Category 2 zone - # class 5 frags	1.0000	0	0	0.69	1.16	-0.60
Category 2 zone - # class 6 frags	1.0000	0	0	0.10	0.32	-0.32
Category 2 zone - # class 7 frags	0.2806	1	3.05	0.33	0.57	1.18
Category 2 zone - # class 8 frags	0.2052	1	4.32	0.23	0.48	1.59
Category 2 zone - # class 9 frags	0.4915	4	1.12	3.56	2.33	0.19
Category 3 zone - # class 1 frags	0.0039	13	3.05	4.26	2.42	3.60
Category 3 zone - # class 3 frags	<0.0001	23	5.14	4.48	2.38	7.77
Category 3 zone - # class 4 frags	0.0341	2	6.56	0.30	0.55	3.06
Category 3 zone - # class 5 frags	0.0950	4	3.22	1.24	1.67	1.66
Category 3 zone - # class 6 frags	0.0004	3	22.29	0.13	0.36	7.87
Category 3 zone - # class 7 frags	0.0811	2	4.27	0.47	0.68	2.25
Category 3 zone - # class 8 frags	0.3699	1	2.20	0.46	0.67	0.82
Category 3 zone - # class 9 frags	0.0009	15	4.06	3.69	2.41	4.70
Category 4 zone - # class 1 frags	0.0371	8	2.48	3.22	2.10	2.28
Category 4 zone - # class 4 frags	0.0206	11	2.47	4.45	2.73	2.40
Category 4 zone - # class 5 frags	0.6357	1	0.72	1.39	1.52	-0.26
Category 4 zone - # class 6 frags	0.1117	1	8.48	0.12	0.34	2.58
Category 4 zone - # class 7 frags	1.0000	0	0	0.41	0.65	-0.63
Category 4 zone - # class 8 frags	1.0000	0	0	0.27	0.51	-0.52
Category 4 zone - # class 9 frags	0.3774	4	1.33	3.02	2.28	0.43
Category 5 zone - # class 5 frags	0.0157	105	1.33	79.96	11.07	2.26
Category 6 zone - # class 5 frags	0.7502	1	0.54	1.85	1.73	-0.49
Category 6 zone - # class 6 frags	0.3501	3	1.45	2.07	1.53	0.61
Category 6 zone - # class 7 frags	0.8061	1	0.54	1.85	1.49	-0.57
Category 6 zone - # class 8 frags	0.7274	1	0.76	1.31	1.15	-0.27
Category 6 zone - # class 9 frags	0.2519	6	1.48	4.06	2.39	0.81
Category 7 zone - # class 5 frags	0.6107	4	0.90	4.46	2.54	-0.18
Category 7 zone - # class 7 frags	0.2374	7	1.46	4.78	2.46	0.90
Category 7 zone - # class 8 frags	1.0000	0	0	0.30	0.55	-0.55
Category 7 zone - # class 9 frags	0.5559	4	0.96	4.18	2.47	-0.07
Category 8 zone - # class 5 frags	0.5048	4	1.05	3.81	2.29	0.08
Category 8 zone - # class 8 frags	0.4209	5	1.20	4.18	2.28	0.36
Category 8 zone - # class 9 frags	0.9648	1	0.24	4.19	2.45	-1.30
Category 9 zone - # class 9 frags	0.0306	156	1.22	127.93	14.06	2.00

Mixed (cat 2 /class 2,3,4 – tx	0.2702	1	3.26	0.31	0.54	1.28
Mixed (cat 2 /class 2,3,4 – non-tx	0.0503	1	19.42	0.05	0.23	4.19
Mixed (cat 2 /class 3,4 – indeterm	0.0888	17	1.93	8.83	5.65	1.45
Mixed (cat 3 /class 3,4 – tx	0.1099	1	8.70	0.11	0.33	2.65
Mixed (cat 3 /class 3,4 – non-tx	0.0793	1	12.03	0.08	0.29	3.16
Mixed (cat 3 /class 3,4 – indeterm	<0.0001	23	5.02	4.58	2.42	7.61
Mixed (cat 4 /class 4 – tx	1.0000	0	0	0.16	0.39	-0.39
Mixed (cat 4 /class 4 – non-tx	1.0000	0	0	0.06	0.24	-0.24
Mixed (cat 4 /class 4 – indeterm	0.0143	11	2.60	4.24	2.67	2.53
Total # transcribed oris	0.0017	62	1.67	37.09	7.83	3.18
Total # non-transcribed	<0.0001	337	1.29	261.22	17.09	4.43
Total # indeterminate	<0.0001	51	2.89	17.65	6.35	5.25
# of fragments in category 1 zone	0.4158	28	1.07	26.25	7.04	0.25
# of fragments in category 2 zone	0.0073	36	2.13	16.88	8.12	2.35
# of fragments in category 3 zone	<0.0001	63	4.19	15.03	5.67	8.46
# of fragments in category 4 zone	0.0311	25	1.94	12.87	5.80	2.09
# of fragments in category 5 zone	0.0157	105	1.31	79.97	11.07	2.26
# of fragments in category 6 zone	0.4384	12	1.08	11.12	4.94	0.18
# of fragments in category 7 zone	0.4196	15	1.09	13.72	5.46	0.23
# of fragments in category 8 zone	0.6773	10	0.82	12.18	5.19	-0.42

C1. Log HeLa (128 zones)	p-value	# actual	fold-change	mean random	sd random	z
1. Fragment in tx gene	0.3730	21	1.08	19.47	3.29	0.47
2. Tx gene(s) in fragment	<0.0001	24	3.50	6.86	2.13	8.06
3. Frag overlaps 5' tx gene(s)	0.0001	22	2.65	8.31	2.54	5.39
4. Frag overlaps 3' tx gene(s)	0.0204	13	1.80	7.24	2.41	2.39
5. Frag in non-tx gene	0.9952	17	0.65	26.06	3.79	-2.40
6.Non-tx gene(s) in frag	0.5155	8	1.04	7.68	2.38	0.13
7. Frag overlaps 5' non-tx gene(s)	0.4366	9	1.10	8.19	2.63	0.31
8. Frag overlaps 3' non-tx gene(s)	0.9805	2	0.37	5.48	2.19	-1.59
9. Intergenic	1.0000	12	0.31	38.70	4.18	-6.39
Total transcribed ori fragments	0.4185	21	1.06	19.83	3.31	0.35
Total free from transcription	1.0000	48	0.56	86.22	4.15	-9.22
Total indeterminate fragments	<0.0001	59	2.69	21.94	3.49	10.61
Mixed (2, 3, 4) transcribed oris	1.0000	0	0	0.36	0.59	-0.62
Mixed (class 2, 3, 4) non-tx	1.0000	0	0	0.11	0.32	-0.33
Mixed (class 2, 3, 4) indeterm	<0.0001	59	2.69	21.94	3.49	10.61

C2. Log GM (177 zones)	p-value	# actual	fold-change	mean random	sd random	z
1. Fragment in tx gene	1.0000	12	0.19	63.04	6.07	-8.41
2. Tx gene(s) in fragment	<0.0001	12	4.27	2.81	1.52	6.06
3. Frag overlaps 5' tx gene(s)	<0.0001	23	2.26	10.18	2.91	4.40
4. Frag overlaps 3' tx gene(s)	0.6808	9	0.91	9.92	2.89	-0.32
5. Frag in non-tx gene	1.0000	42	0.27	158.37	8.17	14.24
6. Non-tx gene(s) in frag	0.9194	4	0.61	6.64	2.34	-1.13
7. Frag overlaps 5' non-tx gene	0.9956	7	0.46	15.27	3.55	-2.33
8. Frag overlaps 3' non-tx gene	0.9985	5	0.37	13.65	3.34	-2.59
9. Intergenic	1.0000	63	0.24	258.11	8.87	-22.00
Total transcribed ori fragments	1.0000	13	0.21	63.79	6.09	-8.34
Total free from transcription	1.0000	121	0.27	452.34	6.73	-49.21
Total indeterminate fragments	0.0001	43	1.97	21.87	4.07	5.20
Mixed (2, 3, 4) transcribed oris	0.5316	1	1.34	0.75	0.85	0.30
Mixed (class 2, 3, 4) non-tx	1.0000	0	0	0.30	0.54	-0.55
Mixed (class 2, 3, 4) indeterm	0.0001	43	1.97	21.87	4.07	5.20

Table SIV - Fixed Isolated & Zones – Randomization for histone marks (10k iterations)

A. Log HeLa (277 isolated)		p-value	# actual	fold-change	mean random	sd random	z
1	±2 kb TSS – Hp*/Tx	< 0.0001	87	1.43	60.95	5.42	4.81
2	±2 kb TSS - Hp^{o}/Tx	0.7948	3	0.80	3.74	1.48	-0.50
3	±2 kb TSS - Hp*/non-Tx	0.0065	80	1.24	64.76	5.99	2.54
4	±2 kb TSS - Hp^{o}/non-Tx	0.9999	20	0.59	33.98	4.35	-3.21
5	5' - H*	0.6542	6	0.91	6.57	2.42	-0.23
6	5' - H^{o}	1.0000	0	0	1.04	0.99	-1.05
7	3' - H*	0.1126	2	3.44	0.58	0.75	1.90
8	3' - H^{o}	1.0000	0	0	0.18	0.42	-0.43
9	Intergenic - H*	0.2398	56	1.09	51.58	5.54	0.80
10	Intergenic - H^{o}	1.0000	23	0.43	53.62	5.40	-5.67
							100%
11	In gene – H^{o}	0.6194	50	0.97	51.33	5.62	-0.24
12	In gene – H* but no Hp*	0.8282	13	0.83	15.74	3.38	-0.81
13	In gene – H* and Hp*	0.0001	127	1.32	96.36	6.65	4.61
							100% of "In gene"
14	In gene - H* and non-Tx	0.0364	75	1.18	63.39	6.06	1.92

B. Log HeLa (128 zones)		p-value	# actual	fold-change	mean random	sd random	z
1	±2 kb TSS – Hp*/Tx	< 0.0001	75	1.87	40.17	4.03	8.64
2	±2 kb TSS - Hp^{o}/Tx	0.0062	5	2.92	1.71	1.04	3.16
3	±2 kb TSS - Hp*/non-Tx	0.7376	32	0.93	34.28	4.31	-0.53
4	±2 kb TSS - Hp^{o}/non-Tx	1.0000	4	0.30	13.14	2.90	-3.15
5	5' - H*	1.0000	0	0	3.06	1.69	-1.82
6	5' - H^{o}	1.0000	0	0	0.50	0.69	-0.73
7	3' - H*	1.0000	0	0	0.32	0.57	-0.57
8	3' - H^{o}	1.0000	0	0	0.13	0.35	-0.36
9	Intergenic - H*	0.9994	10	0.48	20.91	3.53	-3.09
10	Intergenic - H^{o}	1.0000	2	0.15	13.77	3.08	-3.82
							100%
11	In gene – H^{o}	0.9894	8	0.55	14.54	3.24	-2.02
12	In gene – H* but no Hp*	0.9824	4	0.48	8.32	2.49	-1.73
13	In gene – H* and Hp*	< 0.0001	104	1.57	66.44	4.57	8.22
							100% of "In gene"
14	In gene - H* and non-Tx	0.9209	31	0.84	36.73	4.43	-1.30

C. Log GM (538 isolated)		p-value	# actual	fold-change	mean random	sd random	z
1	±2 kb TSS - Hp*/Tx	0.1852	83	1.08	76.67	6.58	0.96
2	±2 kb TSS - Hp°/Tx	0.9680	6	0.65	9.28	2.10	-1.57
3	±2 kb TSS - Hp*/non-Tx	0.4398	154	1.01	152.30	8.37	0.20
4	±2 kb TSS - Hp°/non-Tx	0.9593	34	0.82	41.64	4.69	-1.63
5	5' - H*	0.7221	12	0.88	13.61	3.45	-0.47
6	5' - H°	0.1894	3	1.97	1.52	1.18	1.25
7	3' - H*	0.1371	4	1.98	2.02	1.34	1.47
8	3' - H°	1.0000	0	0	0.68	0.79	-0.86
9	Intergenic - H*	0.0343	163	1.11	147.35	8.39	1.87
10	Intergenic - H°	0.9792	79	0.85	92.93	7.22	-1.93
							100%
11	In gene – H°	0.9994	47	0.68	69.35	6.63	-3.37
12	In gene – H* but no Hp*	0.8776	25	0.85	29.30	4.14	-1.04
13	In gene – H* and Hp*	0.0060	205	1.13	181.25	8.99	2.64
							100% of "In gene"
14	In gene – H* & non-Tx	0.0596	149	1.10	135.52	8.30	1.62

D. Log GM (177 zones)		p-value	# actual	fold-change	mean random	sd random	z
1	±2 kb TSS - Hp*/Tx	<0.0001	55	1.71	32.13	4.19	5.45
2	±2 kb TSS - Hp°/Tx	0.9105	1	0.54	1.86	1.07	-0.80
3	±2 kb TSS - Hp*/non-Tx	0.8428	49	0.91	53.78	5.19	-0.92
4	±2 kb TSS - Hp°/non-Tx	0.9930	9	0.58	15.59	3.07	-2.15
5	5' - H*	0.3870	5	1.23	4.08	1.92	0.48
6	5' - H°	1.0000	0	0	0.43	0.63	-0.67
7	3' - H*	0.4004	1	1.97	0.51	0.70	0.70
8	3' - H°	1.0000	0	0	0.09	0.29	-0.30
9	Intergenic - H*	0.9565	40	0.84	47.80	4.89	-1.59
10	Intergenic - H°	0.8715	17	0.82	20.75	3.79	-0.99
							100%
11	In gene – H°	1.0000	3	0.16	18.28	3.73	-4.10
12	In gene – H* but no Hp*	0.7783	9	0.85	10.56	2.65	-0.59
13	In gene – H* and Hp*	<0.0001	102	1.37	74.51	5.41	5.08
							100% of "In gene"
14	In gene – H* & non-TX	0.3903	56	1.04	54.03	5.31	0.37

Table SV – Locations of overlapping HeLa bubbles, NS (Prioleau), & NS (Dutta)

SIGNAL		GENE(S)				REMARKS
Chr	**Co-ordinates**	**Name**	**Chr**	**Co-ordinates**	**Strand**	
ChrX	122820116-122823175	BX640970	ChrX	122820089-122960880	+	Ori fragment entirely within a tx gene
Chr7	115755434-115765854	AF172085	Chr7	115760357-115793619	+	Ori fragment overlaps 5' of tx gene(s)
		NM_001753	Chr7	115758789-115795181	+	
Chr7	116093377-116102261	NM_006136	Chr7	116096513-116153263	+	Ori fragment overlaps 5' of tx gene(s)
Chr7	116169990-116190930	AF234882	Chr7	116187345-116464022	+	Ori fragment overlaps 5' of tx gene(s)
		BC030954	Chr7	116187505-116464024	+	
		NM_018412	Chr7	116187331-116464024	+	
ChrX	152882465-152892047	BX538060	ChrX	152884024-152816531	-	Ori fragment overlaps 5' of tx gene(s)
		NM_004992	ChrX	152883976-152808110	-	
Chr15	41846946-41851763	NM_005313	Chr15	41825940-41851036	+	Ori fragment overlaps 3' of tx gene(s)
Chr7	26922870-26927164	NM_153631	Chr7	26939879-26919048	-	Ori fragment entirely within a non tx gene
Chr7	26927170-26938946	NM_153631	Chr7	26939879-26919048	-	Ori fragment entirely within a non tx gene
Chr6	41540995-41548454					Intergenic
ChrX	153131198-153139274					Intergenic