

Short Communication

Involvement of CTCF-Mediated Chromatin Loop Structure in Transcription of Clustered G1 Genes after Mitosis

Ataru Uehara, Shunya Goto, Masashi Fukuoka, Masaya Ohtsu, Katsuya Niki, Dai Kato, Shu-ichiro Kashiwaba and Yasufumi Murakami*

Department of Biological Science and Technology, Tokyo University of Science, Japan

*Corresponding author

Yasufumi Murakami, Department of Biological Science and Technology, Faculty of Industrial Science and Technology, Tokyo University of Science, 6-3-1 Niijuku, Katsushika-ku, Tokyo, Japan ; Tel: 81-3-5876-1717; Fax: 81-3-5876-1470; E-mail: yasufumi@rs.noda.tus.ac.jp

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Abstract

In mammalian cells, transcription is globally silenced during mitosis owing to the highly-condensed chromatin. Immediately after mitosis, daughter cells restart the transcription of early G1 genes along the program which is transmitted from parental cells. Although several mechanisms (such as "mitotic gene bookmarking") have been postulated, the detailed mechanism of transcription of early G1 genes is still unknown. Recently, we have identified 298 genes as the early G1 genes by a genome-wide analysis using nascent mRNA, and found that neighboring genes of early G1 genes are frequently up-regulated at G1 phase subsequent to transcription of the early G1 genes. It has been shown that chromatin loop structure is involved in transcription of clustered genes. Here, we show that CTCF-mediated chromatin loop structure around early G1 gene loci is retained from interphase to mitosis. The retained chromatin loop structure allows G1 genes, which are located nearby the early G1 gene loci, to be three-dimensionally in close proximity to one another and facilitates transcription of these genes in G1 phase. Furthermore, down-regulation of CTCF causes delay of M/G1 transition and decreased transcription of early G1 and G1 genes. Our findings may provide a new insight into the mitotic transmission of transcriptional program to the daughter cells.

ABBREVIATIONS

3C: Chromosome Conformation Capture; CTCF: CCCTC-binding Factor; qRT-PCR: Quantitative Reverse Transcription Polymerase Chain Reaction; siRNA: Small Interfering RNA

INTRODUCTION

Transcription is regulated by numerous factors such as RNA polymerase, transcription factors and epigenetic changes. Basal transcription factor and RNA polymerase II are sequence-specifically recruited to upstream regions of target genes. The epigenetic changes include DNA methylation and histone modifications play an important role in the maintaining of gene expression patterns through DNA replication and mitosis [1,2]. In addition, chromatin loop structure is also involved in gene activation, repression and insulation [3,4].

Transcription of the genes which are expressed in interphase is globally silenced during mammalian mitosis [5, 6]. Generally, the transcriptionally silent state occurs when the chromosomes

condense and when RNA polymerase II and other transcription factors dissociate from the chromatin [7]. At the end of mitosis, these factors are reloaded onto the chromatin after relaxation of the chromosomes. Thus, transcription of the genes that are expressed in interphase is reactivated in daughter nuclei in G1 phase.

In addition to a small number of known early G1 genes, research on the regulatory mechanisms of early G1 gene expression is not fully understood. However, one known mechanism termed "mitotic gene bookmarking" has been described [8]. During mitosis, mitotic gene bookmarking factors such as HSF2 [9], MLL [10], RUNX2 [11], and TBP [12] remain bound to the sequence specific sites of early G1 genes. This binding permits the genes to be maintained in a transcriptionally active state [8].

We previously established a method of genome-wide analysis using nascent mRNAs specifically isolated from living mammalian cells [13]. Conventional genome-wide analysis of the M/G1 transition based on total mRNA has been performed

[14]. However, a weakness of conventional microarray analysis in detecting changes of early G1 genes lies in the abundance of mRNAs carried over from the previous cell cycle, and nascent mRNA levels of the majority of the genes in daughter cells seem to be low in comparison to parental cells. If small changes in nascent mRNA levels in early G1 phase could be detected comprehensively, it should be possible to precisely identify early G1 genes on a genome-wide scale. In our method, cells were cultured in medium containing bromouridine (BrU), which substitutes the 5' of uridine for bromine, and cellular nascent RNAs are BrU-labeled. The nascent RNAs are then specifically isolated by immunoprecipitation using an anti-BrdU antibody. This method enables us to precisely analyze the genome-wide expression profiles of early G1 genes.

We previously obtained detailed expression profiles during the M/G1 transition and identified a variety of early G1 genes and discovered early G1 genes cluster [15]. We performed genome-wide analysis of early G1 genes using nascent mRNA and analyzed the common properties of the genes. We could detect variation in expression level of genes only in our analysis system for nascent mRNA and also obtained detailed expression profiles during the M/G1 transition, and identified variety of early G1 genes. With respect to the relationship between early G1 genes and genomic regions, we discovered that genes in the neighborhood of early G1 genes were frequently up-regulated in G1 phase.

The multi-functional transcription regulator CCCTC-binding factor (CTCF) mediates chromatin looping between its binding sites [16, 17]. CTCF was firstly described as a transcriptional repressor [18], but a function of CTCF in gene regulation was also discovered as a transcriptional activator [19, 20]. Like other transcription factors, CTCF appears to bind to intergenic sequences, often at a distance from the transcriptional start site (TSS) [16]. Multiple highly conserved CTCF-binding sites have been identified in some regions, including human HOXA cluster. CTCF controls HOXA cluster silencing and mediates PRC2-Repressive higher-order chromatin structure in NT2/D1 Cells [21]. In this study, we performed 3C assay to evaluate the spatial proximity between distal chromatin sites and demonstrated that the chromatin loop structure of interphase around the region of early G1 genes is retained until mitosis. We also demonstrated that CTCF is required for the retention and the reactivation of early G1 and G1 genes. Our findings suggest that the transcriptional memory is mediated by chromatin structure and also provide a new insight into mitotic gene bookmarking.

MATERIALS AND METHODS

Cell culture of tsFT210 cells

tsFT210 cells, a Cdc2 temperature sensitive mutant strain of mouse mammary FM3A cells [22], were cultured in RPMI 1640 Medium (Life Technologies, CA, USA) with 10% bovine serum (Life Technologies) which was dialyzed, 0.1 mM MEM non-essential amino acid (Life Technologies), 100 U/ml penicillin, and 100 mg/ml streptomycin (Life Technologies) at 32°C in 5% CO₂.

Cell synchronization

tsFT210 cells were arrested in the G2 phase by incubation for 17 h at a non-permissive temperature (39°C). Secondly,

for mitotic arrest, G2 arrested cells were treated with 50 nM nocodazole (Sigma-Aldrich, MO, USA) for 7 h at a permissive temperature (32°C), followed by two washes with PBS (-), and then cells were cultured at 2.0 x10⁵ cells/ml.

siRNA treatment

siRNA treatment was performed to knockdown *Ctcf* expression in tsFT210 cells. siRNAs specific for *Ctcf* were transfected into 2.5 × 10⁵ cells using Lipofectamine RNAi MAX (Life Technologies). Stealth™ RNAi Negative Control Medium GC Duplexes #2 (Life Technologies) was transfected as a negative control. After transfection, cells were incubated at 32°C for 48 h with one medium change at 7 h after transfection.

Chromosome Conformation Capture (3C) Assay

tsFT210 cells were cross-linked with RPMI 1640 medium supplemented with 1% paraformaldehyde. Cells were lysed and chromatin was digested overnight with 500 units of *EcoRI* (TaKaRa Bio Inc., Shiga, Japan) at 37°C. Digested DNA were ligated for 4 h with 1200 units of T4 DNA ligase (New England Bio-labs, MA, USA) at 16°C. Ligated DNA were purified by phenol chloroform mixture extraction and ethanol precipitation and 3C products were quantified by real-time PCR. Primers used in 3C assay are listed in (Table 1).

Flow cytometry

tsFT210 cells arrested or released from arrest, were fixed with 70% EtOH in staining buffer (3% FBS, 0.1% sodium azide in PBS (-)) for at least 4 h at -20°C. Fixed cells were washed with staining buffer and then labeled with PBS (-) containing 50 µg/ml propidium iodide (Sigma-Aldrich) in the dark. Analysis of DNA content was performed by measuring the intensity of the fluorescence produced by propidium iodide using the FACScalibur instrument (Beckton Dickinson, CA, USA).

Analysis of transcriptional reactivation of G1 genes nearby early G1 gene loci

tsFT210 cells were arrested in mitosis, and release by washes with PBS (-), and then cells were cultured at 2.0 x 10⁵ cells/ml. After release, the cells were treated with BrU for 30 min before harvesting, and were collected every 1 h for 3 h to obtain nascent mRNA during the M/G1 transition.

Transcriptional reactivation of G1 genes nearby early G1 gene loci were analyzed by qRT-PCR with specific primers: *Surf4* [forward: 5'-GCAGTACATGCAGCTTGGAG-3'; reverse: 5'-AGCTGT-GCCCAATGTTTC-3'], and *Med22* [forward: 5'-CCCATCCTTAG-GTTCAGGTTTC-3'; reverse: 5'-GGCAGAGACATTTATGCTCCA-3']. Immunoprecipitation of BrU-labeled RNA, cDNA synthesis, quantitative RT-PCR, were performed as previously described [13, 15].

RESULTS AND DISCUSSION

Chromatin structure of interphase is retained until mitosis at neighboring regions of early G1 genes. Our previous study suggested that the regions of the genes which are up-regulated in G1 phase may be transcriptionally controlled as cluster units. Chromatin loop structure, which brings distal genomic loci into close spatial proximity, is known to be critically involved in the transcription of clustered genes [23-25]. To identify how

Table 1: Sequences of primers used in 3C assay.

Gene area	Primer name	Sequence (5'→3')
Around <i>Surf4</i>	A-14622	TCCCTTTTCACCAATTCAGC
Around <i>Surf4</i>	A-15610	TAAATGAGGGTGGCTGATGG
Around <i>Surf4</i>	A-34382	AGAACTAGCATGGCCTGAGC
Around <i>Surf4</i>	A-35310	ATACAGGGGCAGAAGCAATG
Around <i>Surf4</i>	A-37205	CCTGGGACCTTGAGAATAC
Around <i>Surf4</i>	A-44899	ACCCTGGTAACAGCCATCAG
	(Anchor)	
Around <i>Surf4</i>	A-51216	ACCACTGGGCCAATTTATTC
Around <i>Surf4</i>	A-56927	GACCACCTTCCCATAGCATC
Around <i>Surf4</i>	A-69425	TTTCAGAGACGGTCGTCCAC
Around <i>Surf4</i>	A-75334	GCACACTTTGGAAGCATGAG
Around <i>Psm4</i>	B-12827	TTTCTAAAGCCCAGGCAAGA
Around <i>Psm4</i>	B-18545	TAGAGGCCCTAGCCAGAAGG
Around <i>Psm4</i>	B-43200	GCACAGGCAGGCTAGATTAAC
Around <i>Psm4</i>	B-49143	GCCACCTGGTCTATCTGAG
Around <i>Psm4</i>	B-69348	ACCTTTTCTGGGGTCAAAG
	(Anchor)	
Around <i>Psm4</i>	B-88582	TTCAAAGCCAACCAATACGG
Around <i>Psm4</i>	B-113939	AGACTAGCGGGGCGAGTAAC
Around <i>Psm4</i>	B-132684	TCTACGGTGGCTCAGTAGGC
Around <i>Psm4</i>	B-149786	GCTGCTCTCCGTCTTGTAGC

transcription of early G1 genes is regulated, we firstly compared chromatin structure of the neighboring regions of early G1 genes between asynchronous and mitotic tsFT210 cells. For this purpose, we performed Chromosome Conformation Capture (3C) assay, a powerful tool for analyzing three-dimensional spatial proximity of distal genomic regions. We previously found that *Surf4* and *Psm4* were up-regulated in early G1 phase, and a part of genes located nearby these two genes were up-regulated in G1 phase. In these genomic regions, patterns of relative cross-linking frequencies were mostly similar between asynchronous and mitotic cells (Figure 1A and 1B). On the other hand, the pattern of relative cross-linking frequency of mitotic cells were strikingly different from that of asynchronous cells at the region of genes, which were not up-regulated in G1 phase, although they are located nearby *Surf4*. These results suggest that chromatin structure of interphase is retained until mitosis at the region of the genes, which are located nearby early G1 phase, and up-regulated subsequent to transcription of early G1 phase.

CTCF participates in chromatin loop formation around early G1 genes at mitosis

Previous studies have shown that the CCCTC-binding factor (CTCF) mediates formation of chromatin loop and regulates transcription [17, 26]. Thus, we next investigated whether CTCF are also involved in chromatin loop formation around early G1 genes. We depleted CTCF in tsFT210 cells by siRNA and analyzed chromatin structure of *Surf4* locus in asynchronous and synchronized cells. We could not observe any significant difference in pattern of cross-linking frequency at the region of genes which were up-regulated in G1 phase between control and CTCF-depleted cells in asynchronous cells (Figure 2A). This result indicates that down-regulation of CTCF does not change

chromatin structure of these genomic regions in interphase cells. However, in mitotic cells, CTCF-depleted cells showed distinct difference in chromatin structure of same regions from that of control cells (Figure 2B). Although CTCF mediates chromatin loop formation, depletion of CTCF largely up-regulated the cross-linking frequency in these regions. Therefore, we suppose that the defect of CTCF caused incorrect chromatin loop formation, and it led to abnormal transcription of early G1 and G1 genes. On the other hand, depletion of CTCF affects chromatin structure of the region of the genes which are not up-regulated in G1 in both asynchronous and mitotic cells. Taken together, our data suggest that CTCF participates in chromatin loop formation around early G1 genes in mitosis, but the effect is small in interphase.

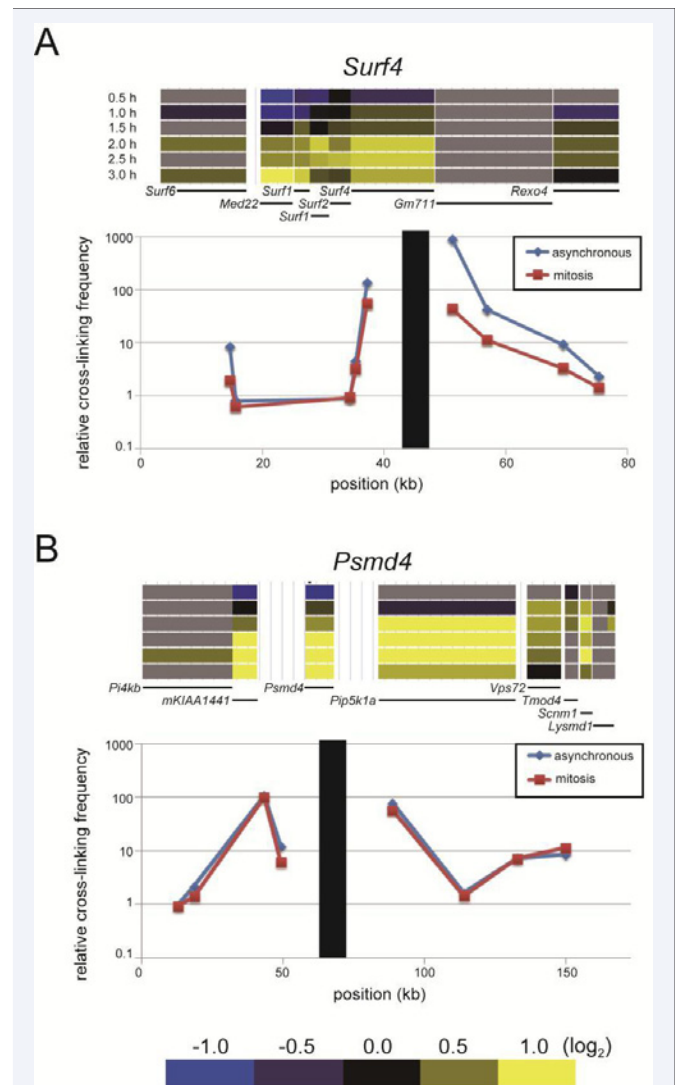


Figure 1 Chromatin structure around early G1 gene loci is retained from interphase to mitosis. Chromatin interaction between early G1 and their neighboring genes loci were analyzed by 3C assay in asynchronous and mitotic tsFT210 cells. (A) Specific primers against the region of early G1 genes (A) *Surf4*, (B) *Psm4* and their neighboring regions were used in quantitative PCR. Colored boxes represent transcriptional levels of the genes which are located in these loci at each time point after nocodazole release. Gray boxes mean below the limit of detection. Black bars indicate positions of anchor primers.

CTCF controls transcriptional reactivation of G1 genes nearby early G1 gene loci

It has been shown that down-regulation of CTCF affects in gene expression both positively and negatively [27], accordingly, we next examined the effect of the depletion of CTCF in transcription of early G1 and G1 genes. To obtain expression profile of the genes correctly, we labeled nascent mRNAs in cells with BrU and collected by immunoprecipitation using anti-BrdU antibody. After cDNA synthesis, expression levels of *Surf4* and *Med22* were analyzed by quantitative PCR. As shown in Figure 3A, we observed significant decrease of transcription of early G1 gene *Surf4* in CTCF-depleted cells compared to control cells.

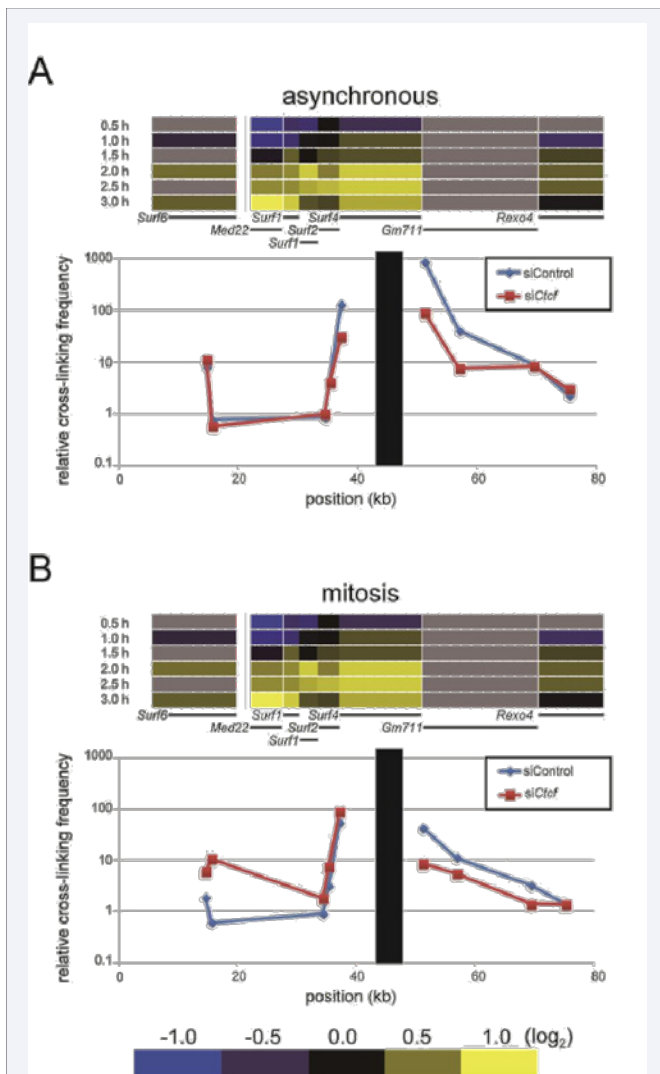


Figure 2 Retention of chromatin loop structure of G1 genes nearby early G1 genes is mediated by CTCF. tsFT210 cells were transfected with siRNA against *Ctcf* and chromatin interactions were then analyzed in (A) asynchronous and (B) mitotic cells. Colored boxes represent transcriptional levels of the genes which are located in these loci at each time point after nocodazole release. Colored boxes represent transcriptional levels of the genes which are located in these loci at each time point after nocodazole release. Gray boxes mean below the limit of detection. Black bars indicate positions of anchor primers.

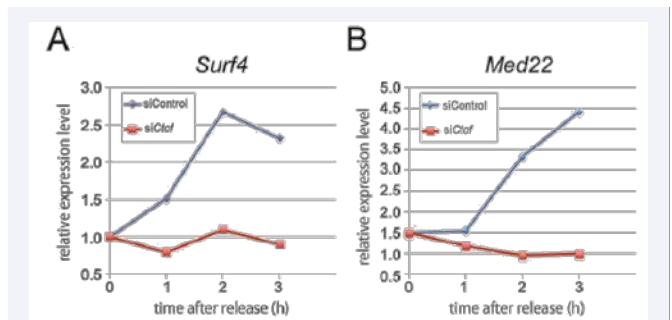


Figure 3 CTCF is required for the transcription of G1 genes nearby early G1 genes. CTCF-depleted tsFT210 cells were synchronized in mitosis. Cells were then released and labeled with BrU for 30 minutes before harvest. Nascent mRNAs were prepared from the collected cells by immunoprecipitation using anti-BrdU antibody, then transcription levels of (A) *Surf4* and its neighboring gene (B) *Med22*, were analyzed by quantitative RT-PCR.

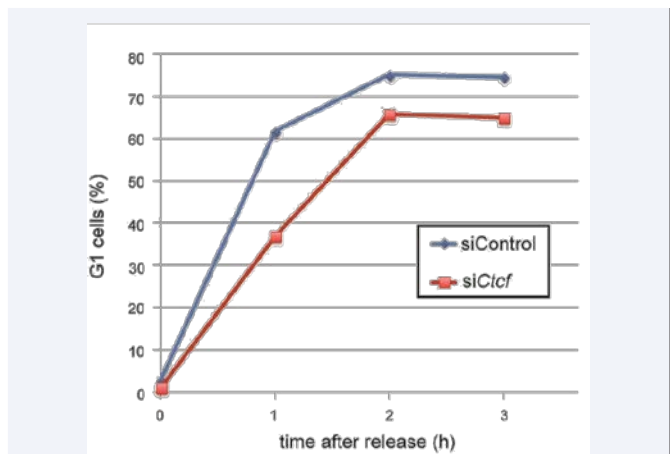


Figure 4 CTCF is involved in G1/M transition. tsFT210 cells were transfected with siRNA against *Ctcf* and then synchronized in mitosis. After release from mitosis, cells were collected at the indicate time points and analyzed by flow cytometry.

Furthermore, depletion of CTCF also decreased the transcription of a G1 gene, *Med22*, which is located in the vicinity of *Surf4* locus (Figure 3B). These results suggest that correct chromatin structure mediated by CTCF is required for the transcription of early G1 and their neighboring G1 genes. To exclude the possibility that the suppression of these genes may be caused by delay of mitosis in CTCF-depleted cells, we investigated whether depletion of CTCF affects in G1/M transition. Twenty-four hours after siRNA transfection, we synchronized tsFT210 cells at mitosis and then released the blockage. More than sixty percent of control cells, but only thirty percent of CTCF-depleted cells were detected in G1 phase fraction at one-hour after nocodazole release (Figure 4A and 4B). Depletion of CTCF did not affect the efficiency of synchronization and the cell cycle distribution of asynchronous cells (data not shown). Because G1 fraction reached to sixty percent at two hours after release in CTCF-depleted cells, depletion of CTCF may delay M/G1 transition for about one hour. As shown in Figure 3A and 3B, suppression of *Surf4* and *Med22* persisted for at least three hours, thus we

suppose that the suppression of early G1 and G1 genes in CTCF-depleted cells may be due to the incorrect chromatin structure but the delay of M/G1 transition.

CONCLUSION

In this study, we found that the chromatin loop structure of early G1 genes and their neighboring G1 genes is retained until mitosis, and this retention enables these genes to be transcribed in early G1 and G1 phase, respectively. Because histone modifications, such as methylation and acetylation [28-31], are thought to be involved in the regulation of transcription of early G1 genes, it is possible that specific pattern of histone modifications is required to prevent the chromatin structure around early G1 genes from chromatin rearrangement through mitosis. However, further study is needed to address the precise mechanism of retention of chromatin structure around early G1 genes.

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REFERENCES

1. Keshet I, Lieman-Hurwitz J, Cedar H. DNA methylation affects the formation of active chromatin. *Cell*. 1986; 44: 535-543.
2. Cheung P, Allis CD, Sassone-Corsi P. Signaling to chromatin through histone modifications. *Cell*. 2000; 103: 263-271.
3. Dekker J, Rippe K, Dekker M, Kleckner N. Capturing chromosome conformation. *Science*. 2002; 295(5558): 1306-1311.
4. Kagey MH, Newman JJ, Bilodeau S, Zhan Y, Orlando DA, van Berkum NL, et al. Mediator and cohesin connect gene expression and chromatin architecture. *Nature*. 2010; 467: 430-435.
5. Prasanth KV, Sacco-Bubulya PA, Prasanth SG, Spector DL. Sequential entry of components of the gene expression machinery into daughter nuclei. *Mol Biol Cell*. 2003; 14: 1043-1057.
6. Delcuve GP, He S, Davie JR. Mitotic partitioning of transcription factors. *J Cell Biochem*. 2008; 105: 1-8.
7. Martinez-Balbas MA, Dey A, Rabindran SK, Ozato K, Wu C. Displacement of sequence-specific transcription factors from mitotic chromatin. *Cell*. 1995; 83: 29-38.
8. Sarge KD, Park-Sarge OK. Mitotic bookmarking of formerly active genes Keeping epigenetic memories from fading. *Cell Cycle*. 2009; 8: 818-823.
9. Wilkerson DC, Skaggs HS, Sarge KD. HSF2 binds to the Hsp90, Hsp27, and c-Fos promoters constitutively and modulates their expression. *Cell Stress Chaperones*. 2007; 12: 283-290.
10. Blobel GA, Kadauke S, Wang E, Lau AW, Zuber J, Chou MM, et al. A reconfigured pattern of MLL occupancy within mitotic chromatin promotes rapid transcriptional reactivation following mitotic exit. *Mol Cell*. 2009; 36: 970-983.
11. Young DW, Hassan MQ, Yang XQ, Galindo M, Javed A, Zaidi SK, et al. Mitotic retention of gene expression patterns by the cell fate-determining transcription factor Runx2. *Proc Natl Acad Sci U S A*. 2007; 104: 3189-3194.
12. Xing H, Vanderford NL, Sarge KD. The TBP-PP2A mitotic complex bookmarks genes by preventing condensin action. *Nat Cell Biol*. 2008; 10: 1318-1323.
13. Ohtsu M, Kawate M, Fukuoka M, Gunji W, Hanaoka F, Utsugi T, et al. Novel DNA microarray system for analysis of nascent mRNAs. *DNA Res*. 2008; 15: 241-251.
14. Beyrouthy MJ, Alexander KE, Baldwin A, Whitfield ML, Bass HW, McGee D, et al. Identification of G1-Regulated Genes in Normally Cycling Human Cells. *PLoS One*. 2008; 3: e3943.
15. Fukuoka M, Uehara A, Niki K, Goto S, Kato D, Utsugi T, et al. Identification of preferentially reactivated genes during early G1 phase using nascent mRNA as an index of transcriptional activity. *Biochem Biophys Res Commun*. 2013; 430: 1005-1010.
16. Kim TH, Abdullaev ZK, Smith AD, Ching KA, Loukinov DI, Green RD, et al. Analysis of the vertebrate insulator protein CTCF-binding sites in the human genome. *Cell*. 2007; 128: 1231-1245.
17. Splinter E, Heath H, Kooren J, Palstra RJ, Klous P, Grosveld F, et al. CTCF mediates long-range chromatin looping and local histone modification in the beta-globin locus. *Genes Dev*. 2006; 20: 2349-2354.
18. Lobanenkov VV, Nicolas RH, Adler VV, Paterson H, Klenova EM, Polotskaja AV, et al. A novel sequence-specific DNA binding protein which interacts with three regularly spaced direct repeats of the CCCTC-motif in the 5'-flanking sequence of the chicken c-myc gene. *Oncogene*. 1990; 5: 1743-1753.
19. Klenova EM, Nicolas RH, Paterson HF, Carne AF, Heath CM, Goodwin GH, et al. CTCF, a conserved nuclear factor required for optimal transcriptional activity of the chicken c-myc gene, is an 11-Zn-finger protein differentially expressed in multiple forms. *Mol Cell Biol*. 1993; 13: 7612-7624.
20. Filippova GN, Fagerlie S, Klenova EM, Myers C, Dehner Y, Goodwin G, et al. An exceptionally conserved transcriptional repressor, CTCF, employs different combinations of zinc fingers to bind diverged promoter sequences of avian and mammalian c-myc oncogenes. *Mol Cell Biol*. 1996; 16: 2802-2813.
21. Farrell CM, West AG, Felsenfeld G. Conserved CTCF insulator elements flank the mouse and human beta-globin loci. *Mol Cell Biol*. 2002; 22: 3820-3831.
22. Th'ng JPH, Wright PS, Hamaguchi J, Lee MG, Norbury CJ, Nurse P, et al. The FT210 cell line is a mouse G2 phase mutant with a temperature-sensitive CDC2 gene product. *Cell*. 1990; 63: 313-324.
23. Mishiro T, Ishihara K, Hino S, Tsutsumi S, Aburatani H, Shirahige K, et al. Architectural roles of multiple chromatin insulators at the human apolipoprotein gene cluster. *EMBO J*. 2009; 28: 1234-1245.
24. Murrell A, Heeson S, Reik W. Interaction between differentially methylated regions partitions the imprinted genes Igf2 and H19 into parent-specific chromatin loops. *Nat Genet*. 2004; 36: 889-893.
25. Noordermeer D, Leleu M, Splinter E, Rougemont J, De Laat W, Duboule D. The dynamic architecture of Hox gene clusters. *Science*. 2011; 334: 222-225.
26. Ling JQ, Li T, Hu JF, Vu TH, Chen HL, Qiu XW, et al. CTCF mediates interchromosomal colocalization between Igf2/H19 and Wsb1/Nf1. *Science*. 2006; 312: 269-272.
27. Phillips JE, Corces VG. CTCF: master weaver of the genome. *Cell*. 2009; 137: 1194-1211.
28. Valls E, Sanchez-Molina S, Martinez-Balbas MA. Role of histone modifications in marking and activating genes through mitosis. *J Biol Chem*. 2005; 280: 42592-42600.
29. Sarge KD, Park-Sarge OK. Gene bookmarking: keeping the pages open. *Trends Biochem Sci*. 2005; 30: 605-610.

30. Dey A, Nishiyama A, Karpova T, McNally J, Ozato K. Brd4 marks select genes on mitotic chromatin and directs postmitotic transcription. *Mol Biol Cell*. 2009; 20: 4899-4909.
31. Zhao R, Nakamura T, Fu Y, Lazar Z, Spector DL. Gene bookmarking accelerates the kinetics of post-mitotic transcriptional re-activation. *Nat Cell Biol*. 2011; 13: 1295-1304.

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