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EXTRA VIEW

The coupled effect of nucleosome organization on gene transcription level and transcriptional plasticity

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ABSTRACT

Nucleosomes are the fundamental units of eukaryotic chromatin and can modulate the DNA accessibility for transcriptional regulatory elements. Many studies have demonstrated the effect of nucleosome organization on gene transcription level and transcriptional plasticity upon different conditions. Our recent study showed that nucleosome organization also plays an important role in modulating the plasticity of gene transcriptional status in maize. Here, we integrated our findings with previous studies on the role of nucleosome organization in regulation of gene transcription. We highlighted our recent finding that nucleosome organization plays an important role in determining the plasticity of gene transcription, beyond its role in regulating gene transcription level, particularly for intrinsically DNA-encoded nucleosome organization. We also discussed the features of sequence and structure of genes involved in affecting nucleosome organization around genes, as well as the potential mechanisms for overcoming the coupled effect of nucleosome organization on gene transcription level and transcriptional plasticity.

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Introduction

Nucleosome is the fundamental structural unit of eukaryotic chromatin. Since the 147 bp of nucleosomal DNA has to wrap around a core histone octamer to form nucleosome,[1] the sequence properties, particularly the bending characteristics, can influence nucleosome formation by affecting intrinsic histone-DNA interactions.[2,3] Many studies have demonstrated the basic role of DNA sequence in determining genome-wide nucleosome organization, which non-homopolymeric G/C-rich sequences favor nucleosome formation while poly (dA:dT) is intrinsically unfavorable for nucleosome formation.[2,4–7] Besides DNA sequence, the *in vivo* nucleosome occupancy is also affected by cellular factors that can override the nucleosome sequence preferences, including ATP-dependent chromatin remodelers and transcription factors, such as activators, components of the preinitiation complex and RNA polymerase II (Pol II).[3,8] Hence, nucleosome occupancy is highly regulated in the genome, and is often depleted in enhancer, promoter and terminator regions.[3,8]

Since nucleosome occupancy can affect the binding of transcription factors by influencing the accessibility of genome DNA, the modulation of nucleosome occupancy is an important component of gene transcription regulation. High-resolution, genome-wide nucleosome organization studies in yeast,[9–11] human,[12,13] mouse,[14,15] Drosophila,[16] Arabidopsis,[17–19] rice,[19,20] and maize[21,22] have showed that the distribution of nucleosomes around genes is associated with transcription levels. For example, the nucleosome depletion at promoter regions of highly expressed genes is generally more pronounced than that of lowly expressed genes. It has been demonstrated that nucleosome occupancy changes are closely associated with the transcriptional changes in stress response, cell differentiation and reprogramming, as well as age alteration in yeast and mouse.[15,23–26] In addition, it was also showed that nucleosome organization is associated with the capacity of genes to alter their transcription levels upon changing conditions.[27–29] Our recent study in maize suggested that nucleosome organization is associated with the plasticity of gene transcriptional status, which refers

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the capacity of genes to alter their transcriptional status among different tissues.[22] In contrast to constitutive genes, the transcriptional statuses of tissue-specific genes are more plastic and variable among different tissues. The nucleosome organization was demonstrated to be distinct for constitutively and tissue-specifically expressed genes.[22] Overall, these studies suggested that nucleosome organization can involve in regulating both gene transcription level and gene transcriptional plasticity, including the capacity of alteration of gene transcriptional status in different conditions and tissue types. Genes with pronounced nucleosome depletion at both 5′ and 3′ ends tend to be highly expressed and display low transcriptional plasticity. The nucleosome organization could not match well with the regulation of gene transcription level and transcriptional plasticity simultaneously in some situations as genes with high transcriptional plasticity might need to be highly expressed, and genes with low transcriptional plasticity might need to be lowly expressed. How nucleosome organization reconcilably affects both gene transcription level and transcriptional plasticity is not known well. In this review, we integrated our recent findings with previous studies on the role of nucleosome organization in regulating gene transcription, and highlighted our recent finding that nucleosome organization is important for determination of gene transcriptional plasticity, beyond its role in regulating gene transcription level, particularly for intrinsically DNA-encoded nucleosome organization.[22]

Nucleosome organization around genes

The genome-wide map of nucleosome occupancy obtained via sequencing the mononucleosomal DNA generated by micrococcal nuclease digestion (MNase-seq) allows us to explore the features of nucleosome organization around genes. The promoter region just upstream of the transcriptional start site (TSS) often displays low nucleosome occupancy level for a typical gene, and is called nucleosome depleted region (NDR).[3,30,31] The NDR in the 5′ end of gene is generally flanked by two well positioned nucleosomes: −1 and +1 nucleosomes, which located in its upstream and downstream, respectively.[3,30,31] Several well positioned nucleosomes are also observed in downstream of the +1 nucleosome with the degree gradually decreased from 5′ to 3′ end of gene.[3,30,31] To be noted, the −1 nucleosome was observed in yeast,[11] human,[12] mouse, [15] Drosophila,[16] but was not identified in Arabidopsis,[17–19] rice,[19,20] and maize,[22,32] different with the 5′ NDR and +1 nucleosome which are conservatively existed in these species. Nucleosomes are also depleted around the transcriptional termination site (TTS).[11,16,22]. Our recent study in maize showed that there is a well positioned nucleosome located immediately upstream of the 3′ NDR of gene,[22] which is called 3′ −1 nucleosome here to distinguish with −1 nucleosome in 5′ end.

The nucleosome organization in 5′end of gene is closely associated with transcription initiation, as which can affect the binding of transcription initiation elements by modulating the accessibility of DNA. The nucleosome depletion in promoter region is important for the binding of many transcription factors, although some, like pioneering transcription factors, preferentially bind in nucleosome occurred regions.[8,14,30] In addition, Pol II pausing is also closely associated with nucleosome occupancy in 5′ end of gene.[30,31] Study in human showed that the distance of +1 nucleosome to TSS for genes with elongating Pol II is longer than genes with stalled Pol II.[12] The role of NDR and −1 nucleosome in gene 3′ end is unclear, which might contribute the transcription termination as 3′ end is the region involving the stop of transcription elongation and divorce of Pol II from the DNA.[30] The transcription elongating, accompanied by nucleosome eviction and reposition,[3] might also be affected by nucleosome occupancy in gene body.

Correlation between nucleosome organization and gene transcription level

Our recent study in maize showed that compared with lowly expressed genes, highly expressed genes typically displayed more pronounced nucleosome depletion at their promoter and terminator regions, lower nucleosome occupancies in their gene bodies, as well as further distance of +1 nucleosome to the TSSs and 3′ −1 nucleosome to the TTSs,[22] which are consistent with the reports in other species.[9,12–20] This general rule is not only for genes with different transcription levels within one tissue or cell type, it is also consistent with the observation in comparing the nucleosome organization of genes with activated or repressed status in different environments, development stages, ages or tissue types.[15,22–26]

One can imagine that the correlation between nucleosome organization and gene transcription level

might be a result of nucleosome reprogramming during gene transcription. Previous studies have provided evidence that nucleosomes in the promoter of *Pho5* were lost during transcriptional activation in yeast.[33,34] Another study further showed that the dynamic change of nucleosome occupancy was linked to the transcription and chromatin regulators.[35] For instance, the stress-activated TF Msn2p is required for nucleosome eviction from its binding sites by nucleosome remodelers.[35] The −1 nucleosome was not observed in Pol II inactivated mutant also reflects the effect of gene transcription process on nucleosome occupancy change.[36] However, our study in maize suggested that nucleosome organization variation accompanied with the change of gene transcriptional status between shoot and endosperm, including the variation of NDRs intensity and +1 and 3′ −1 nucleosome positions, can only account for part of nucleosome organization difference between genes with different transcription levels in the same tissue.[22] According to the role of DNA sequence in determining nucleosome organization,[4,13,22,37] the features of nucleosome organization difference between highly and lowly expressed genes can be reproduced based on analysis of intrinsically DNA-encoded nucleosome organization.[22] Overall, the reduction of nucleosome occupancy around genes, in particularly at promoter region, and the increase of +1/3′ −1 nucleosome distances to TSS/TTS are associated with the increase of gene transcription.

Correlation between nucleosome organization and gene transcriptional plasticity upon changing conditions and tissue types

In yeast, genes can be broadly categorized into two classes: "growth" genes (also known as housekeeping genes), which are continuously expressed during growth, and "stress" genes, which are dynamically expressed in different stress conditions.[38] Using 12 *Hemiascomycota* yeast species, Tsankov et al. found that growth genes displayed wide and deep NDRs at promoters, distinct with stress genes which NDRs are narrow and shallow (Fig. 1).[39] Although RNA polymerase contributes to nucleosome eviction at promoters, distinct NDRs at promoters of growth and stress genes can still be observed after inactivation of Pol II via a temperature-sensitive mutation,[36] indicating that nucleosome organization variation between the two types of genes is not just a result of transcriptional activation. This raises a question if there is other role of nucleosome organization in gene regulation besides affecting transcription level.

The capacity of genes to alter their transcription levels upon changing conditions is different for growth and stress genes. In contrast to growth genes, stress genes are more sensitive to changing condition. Some studies showed that TATA-containing genes, which are generally stress genes, displayed higher transcriptional plasticity than non-TATA genes.[40–42] The correlation of TATA-box presence and transcriptional plasticity could be explained by the effect of chromatin regulation according a later study.[27] Tirosh et al. suggested that there are two typical promoter structures associated with low and high transcriptional plasticity based on analysis of the correlation between nucleosome organization of yeast genes and their capacity to alter transcription level upon a variety of conditions, including environmental stresses, mutations, and developmental transitions.[29] In contrast to low-plasticity genes, high-plasticity genes tend to have more evenly distributed and dynamic nucleosomes in promoters.[29] It is worth to note that TATA boxes themselves can't increase promoter nucleosome occupancy,[8,29] which suggested that the narrow NDRs in promoters of TATA-containing genes might be mainly determined by cellular trans factors or other unknown mechanism. We recently compared the nucleosome organization of constitutively and tissue-specifically expressed genes in maize, and found that nucleosome organization was also associated with the capacity of genes altering their transcriptional status among different tissues.[22] Constitutive genes, which the plasticity of transcriptional status is lower, tend to have more pronounced 5′ and 3′ NDRs, lower nucleosome occupancy in gene bodies, as well as further +1/3′ −1 nucleosome to TSSs/TTSs as compared with tissue-specific genes (Fig. 1).[22] In summary, nucleosome organization around genes can affect transcriptional plasticity of genes upon changing conditions and tissue types. Nucleosome organization features of typically stress genes allow the dynamic competition between nucleosome assembly and transcription factors binding, and thus

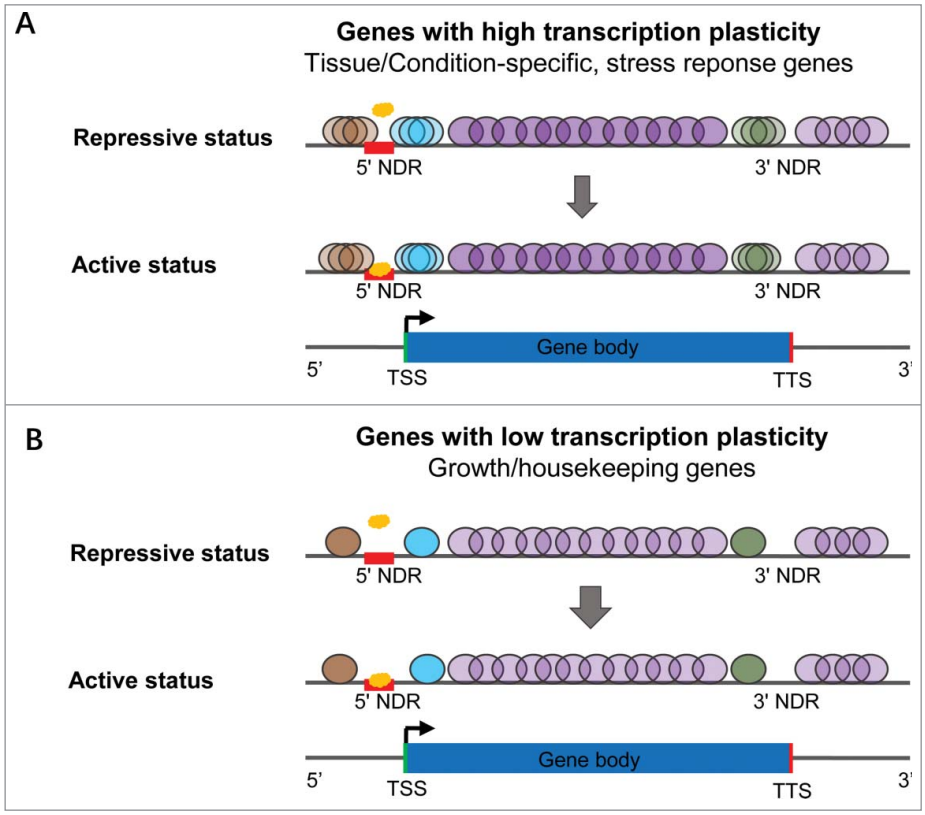

Figure 1. The model of nucleosome organization around genes with high transcriptional plasticity (A) and genes with low transcriptional plasticity (B). Brown, blue, and green circles represent the −1, +1, and 3′ −1 nucleosomes, respectively. As displayed in model, the −1, +1, and 3′ −1 nucleosomes of genes with low transcriptional plasticity are more well positioned than that of genes with high transcriptional plasticity. Yellow and red bulks represent transcription factors and their binding sites, respectively. As displayed in model, the 5′ NDR of genes with low transcriptional plasticity is wider and deeper than that of genes with high transcriptional plasticity, and is more accessible for transcription factors. The deeper purple for genes with high transcriptional plasticity represents their nucleosome occupancy levels are higher than that of genes with low transcriptional plasticity in gene body. The wider gray arrow for genes with low transcriptional plasticity represents their transcription levels tend to be higher than that of genes with high transcriptional plasticity.

contribute to high transcriptional plasticity (Fig. 1).[22,27,29,39]

Role of intrinsically DNA-encoded nucleosome organization in gene transcription

Nucleosome organization *in vivo* is determined by the combination of DNA sequence and cellular *trans* factors.[3] It seems that the role of nucleosome organization guided by cellular *trans* factors can be different with intrinsically DNA-encoded nucleosome organization in gene transcription regulation. Nucleosome organization changes induced by the action of ATP-dependent chromatin remodelers and transcription factors during gene activation are directly associated with gene transcription level change. However, static genome sequence can't encode a nucleosome organization to match with different transcription levels of any given gene. So, what is the key role of intrinsically DNA-encoded nucleosome organization in gene transcription? Study in yeast showed that intrinsic variability of gene transcription in specific environmental cues or stochastic fluctuations is encoded in nucleosome positioning sequences.[28] Although intrinsically DNA-encoded nucleosome organization was associated with transcription level, our recent study showed its association with the capacity of genes to alter their transcriptional status among different tissues is more significant.[22] Genes can display stochastic expression variation within a cell population maintained in a constant environment.[43] This variability of gene expression among individuals in same environment was called as "expression noise", and can also be affected by the intrinsically DNA-encoded nucleosome organization.[43] Interestingly, gene transcriptional plasticity

and expression noise are coupled to some extent.[28,44–47] It was showed that gene transcriptional plasticity can serve as a proxy for noise level, suggesting they might share the same underlining mechanism.[48] Taken together, we propose that the key role of intrinsically DNA-encoded nucleosome organization is determining gene transcriptional plasticity, including stochastic expression noise, rather than gene transcription level.

Lots of DNA sequence and gene structure features affect intrinsically DNA-encoded nucleosome organization around genes. Poly (dA:dT) tracts are enriched in eukaryotic genomes, particularly in promoters.[3] It has been demonstrated that poly (dA:dT) disfavors nucleosomes formation, and the number and the length of which strongly influence nucleosome depletion in gene promoters.[3,49] Compared to stress genes, growth genes display stronger poly (dA:dT) tracts and so more pronounced NDRs in promoters,[39] which contribute to lower transcriptional plasticity of growth genes.[3,29,39] Moreover, a recent study in *Caenorhabditis elegans* suggested that AT content of promoter sequences might influence gene transcriptional plasticity by affecting nucleosome fragility.[50] Upstream distance and gene orientation also affect nucleosome organization.[51] Genes with short upstream distance and head-to-head genes tend to have promoters with low nucleosome occupancy and flanked by strongly positioned nucleosomes.[51] Our recent study in maize revealed that gene transcriptional plasticity is associated with DNA sequence features of gene body too.[22] High AT context of exon and intron sequences contribute to low nucleosome occupancy in gene body.[22] Particularly, we found constitutive genes and tissue-specific genes displayed distinct codon usage as constitutive genes prefer codons with two or three A/T nucleotides, suggesting utilization of codon degeneracy may serve as a mechanism to affect nucleosome organization.[22] The nucleosome occupancy of intron is significantly lower than that of exon, which is consistent with the higher AT context of intron.[22] Interesting, study in human indicated that intronless genes tend to be tissue-specific, reflecting the role of intron number on gene transcriptional plasticity via affecting nucleosome organization.[52] Our study also showed that constitutive genes tend to have longer 5′ and 3′ UTRs than tissue-specific genes, which might play a role in forming longer distance of +1 and 3′ −1 nucleosomes to TSS and TTS, respectively.[22]

Potential mechanisms for overcoming the coupled effect of nucleosome organization on gene transcription level and transcriptional plasticity

As mentioned above, nucleosome organization can affect both gene transcription level and transcriptional plasticity. The typical nucleosome organization of genes with high and low transcriptional plasticity is corresponding to low and high transcription levels, respectively. However, it is logical that high transcription plastic genes might need to be highly expressed, while low transcription plastic genes might need to be lowly expressed,[22] which is inconsistent with the coupled effect of nucleosome organization on gene transcriptional plasticity and expression level. A previous study demonstrated that there are two distinct DNA-encoded strategies for increasing transcription level in yeast, strengthening the binding site of transcription factor which increases transcripts produced from the active state, and adding nucleosome-disfavoring sequences which increases the frequency of promoter transitions between active and inactive states.[53] Compared to the former strategy, the latter strategy likely reduces the transcriptional plasticity of genes.[53] These are consistent with the studies in human that the highly expressed intronless genes, which tend to be tissue-specific genes,[52] require a higher density of Pol II in an elongating state as compared with intron-containing genes.[54] Thus, genes might can partially decoupled the effect of nucleosome organization on transcription level and transcriptional plasticity by harboring different strategies for increasing transcription level.

The translation levels of maize genes have been measured by sequencing the ribosome protected mRNA fragments.[55] Using these data, we found that the translational efficiencies, which measured by the ratio of translation level and transcription level, of constitutive genes are significantly lower than tissue-specific genes.[22] It seems like a fitness cost-benefit conflict that constitutive genes were highly expressed but showed low efficiency of RNA utilization. We propose it might duo to utilization of different strategies for increasing transcription level is not enough for overcoming the coupled effect of nucleosome

organization on transcription level and transcriptional plasticity, as supported by the observation that the transcription level of constitutive genes is significantly higher than tissue-specific genes overall.[22] Therefore, the translational regulation after transcription is also very important for obtaining the final protein abundances, which can overcome the coupled effect of nucleosome organization on gene transcription level and transcriptional plasticity.

Conclusion and future perspectives

Nucleosome organization is an important chromatin feature. The characteristics of nucleosome organization around genes, particularly for promoters, have been revealed in many species. It is demonstrated that nucleosome organization can affect both gene transcription level and transcriptional plasticity by modulating the accessibility of DNA sequence for transcription factors. The role of nucleosome organization in determining gene transcriptional plasticity is likely beyond its role in regulating transcription level, particularly for intrinsically DNA-encoded nucleosome organization. Notably, the nucleosome organization could not be optimal simultaneously for gene transcription level and transcriptional plasticity in some situations, which probably is overcame by the utilization of different strategies for increasing transcription level and the regulation of gene translation. It is interesting to further survey the possible translational regulating factors involve in modulating the final protein abundances. Poly (dA:dT) tracts in promoter, codon usage in exon, and the length of 5′ and 3′ UTRs are associated with intrinsically DNA-encoded nucleosome. Explore how these features were evolved will help to understand the formation of gene regulation diversity during evolution. It is important to mention that nucleosome organization is in fact exceptionally dynamic and complex *in vivo*.[31] Comprehensive analysis of the correlation between the dynamic of nucleosome and gene transcription level is necessary for elucidation of gene transcriptional regulation.

Disclosure of potential conflicts of interest

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References

1. Luger K, Mäder AW, Richmond RK, et al. Crystal structure of the nucleosome core particle at 2.8 Å resolution. Nature. 1997;389(6648):251–260.
2. Segal E, Fondufe-Mittendorf Y, Chen L, et al. A genomic code for nucleosome positioning. Nature. 2006;442(7104):772–778.
3. Struhl K, Segal E. Determinants of nucleosome positioning. Nat Struct Mol Biol. 2013;20(3):267–273.
4. Kaplan N, Moore IK, Fondufe-Mittendorf Y, et al. The DNA-encoded nucleosome organization of a eukaryotic genome. Nature. 2008;458(7236):362–366.
5. Zhang Y, Moqtaderi Z, Rattner BP, et al. Intrinsic histone-DNA interactions are not the major determinant of nucleosome positions in vivo. Nat Struct Mol Biol. 2009;16(8):847–852.
6. Zhang Z, Pugh BF. High-resolution genome-wide mapping of the primary structure of chromatin. Cell. 2011;144(2):175–186.
7. Sexton BS, Avey D, Druliner BR, et al. The spring-loaded genome: nucleosome redistributions are widespread, transient, and DNA-directed. Genome Res. 2014;24(2):251–259.
8. Radman-Livaja M, Rando OJ. Nucleosome positioning: how is it established, and why does it matter? Dev Biol. 2010;339(2):258–266.
9. Lee W, Tillo D, Bray N, et al. A high-resolution atlas of nucleosome occupancy in yeast. Nat Genet. 2007;39(10):1235–1244.
10. Brogaard K, Xi L, Wang J, Widom J. A map of nucleosome positions in yeast at base-pair resolution. Nature. 2012;486(7404):496–501.
11. Mavrich TN, Ioshikhes IP, Venters BJ, et al. A barrier nucleosome model for statistical positioning of nucleosomes throughout the yeast genome. Genome Res. 2008;18(7):1073–1083.
12. Schones DE, Cui K, Cuddapah S, et al. Dynamic regulation of nucleosome positioning in the human genome. Cell. 2008;132(5):887–898.
13. Valouev A, Johnson SM, Boyd SD, et al. Determinants of nucleosome organization in primary human cells. Nature. 2011;474(7352):516–520.
14. Teif VB, Vainshtein Y, Caudron-Herger M, et al. Genome-wide nucleosome positioning during embryonic stem cell development. Nat Struct Mol Biol. 2012;19(11):1185–1192.

15. West JA, Cook A, Alver BH, et al. Nucleosomal occupancy changes locally over key regulatory regions during cell differentiation and reprogramming. Nat Commun. 2014;5:4719.
16. Mavrich TN, Jiang C, Ioshikhes IP, et al. Nucleosome organization in the Drosophila genome. Nature. 2008;453(7193):358–362.
17. Li G, Liu S, Wang J, He J, et al. ISWI proteins participate in the genome−wide nucleosome distribution in Arabidopsis. The Plant Journal. 2014;78(4):706–714.
18. Liu M, Seddon AE, Tsai ZT, et al. Determinants of nucleosome positioning and their influence on plant gene expression. Genome Res. 2015;25(08):1182–1195.
19. Jiang J, Zhang T, Zhang W. Genome-wide nucleosome occupancy and positioning and their impact on gene expression and evolution in plants. Plant Physiol. 2015;168:1406–1416.
20. Wu Y, Zhang W, Jiang J. Genome-Wide Nucleosome Positioning Is Orchestrated by Genomic Regions Associated with DNase I Hypersensitivity in Rice. Plos Genet. 2014;10(5):e1004378.
21. Rodgers-Melnick E, Vera DL, Bass HW, et al. Open chromatin reveals the functional maize genome. Proc Natl Acad Sci. 2016;113(22):E3177–E3184.
22. Chen J, Li E, Zhang X, et al. Genome-wide nucleosome occupancy and organization modulates the plasticity of gene transcriptional status in maize. Mol Plant. 2017;10(7):962–974.
23. Shivaswamy S, Bhinge A, Zhao Y, et al. Dynamic remodeling of individual nucleosomes across a eukaryotic genome in response to transcriptional perturbation. Plos Biol. 2008;6(3):e65.
24. Bochkis IM, Przybylski D, Chen J, et al. Changes in Nucleosome Occupancy Associated with Metabolic Alterations in Aged Mammalian Liver. Cell Rep. 2014;9(3):996–1006.
25. Hu Z, Chen K, Xia Z, et al. Nucleosome loss leads to global transcriptional up-regulation and genomic instability during yeast aging. Gene dev. 2014;28(4):396–408.
26. Sexton BS, Druliner BR, Vera DL, et al. Hierarchical regulation of the genome: global changes in nucleosome organization potentiate genome response. Oncotarget. 2016;7(6):6460–6475.
27. Choi JK, Kim Y. Epigenetic regulation and the variability of gene expression. Nat Genet. 2008;40(2):141–147.
28. Choi JK, Kim Y. Intrinsic variability of gene expression encoded in nucleosome positioning sequences. Nat Genet. 2009;41(4):498–503.
29. Tirosh I, Barkai N. Two strategies for gene regulation by promoter nucleosomes. Genome Res. 2008;18(7):1084–1091.
30. Jiang C, Pugh BF. Nucleosome positioning and gene regulation: advances through genomics. Nat Rev Genet. 2009;10(3):161–172.
31. Lai WK, Pugh BF. Understanding nucleosome dynamics and their links to gene expression and DNA replication. Nat Rev Mol Cell Bio. 2017;18:548–562.
32. Fincher JA, Vera DL, Hughes DD, et al. Genome-Wide Prediction of Nucleosome Occupancy in Maize Reveals Plant Chromatin Structural Features at Genes and Other Elements at Multiple Scales. Plant Physiol. 2013;162(2):1127–1141.
33. Boeger H, Griesenbeck J, Strattan JS, et al. Nucleosomes unfold completely at a transcriptionally active promoter. Mol Cell. 2003;11(6):1587–1598.
34. Reinke H, Hörz W. Histones are first hyperacetylated and then lose contact with the activated PHO5 promoter. Mol Cell. 2003;11(6):1599–1607.
35. Huebert DJ, Kuan P, Keleş S, et al. Dynamic changes in nucleosome occupancy are not predictive of gene expression dynamics but are linked to transcription and chromatin regulators. Mol Cell Biol. 2012;32(9):1645–1653.
36. Weiner A, Hughes A, Yassour M, et al. High-resolution nucleosome mapping reveals transcription-dependent promoter packaging. Genome Res. 2010;20(1):90–100.
37. Zhang Z, Wippo CJ, Wal M, Ward E, et al. A packing mechanism for nucleosome organization reconstituted across a eukaryotic genome. Science. 2011;332(6032):977–980.
38. Rando OJ, Winston F. Chromatin and transcription in yeast. Genetics. 2012;190(2):351–387.
39. Tsankov AM, Thompson DA, Socha A, et al. The role of nucleosome positioning in the evolution of gene regulation. Plos Biol. 2010;8(7):e1000414.
40. Landry CR, Lemos B, Rifkin SA, et al. Genetic properties influencing the evolvability of gene expression. Science. 2007;317(5834):118–121.
41. Tirosh I, Weinberger A, Carmi M, et al. A genetic signature of interspecies variations in gene expression. Nat Genet. 2006;38(7):830.
42. Basehoar AD, Zanton SJ, Pugh BF. Identification and distinct regulation of yeast TATA box-containing genes. CELL. 2004;116(5):699–709.
43. Sharon E, van Dijk D, Kalma Y, et al. Probing the effect of promoters on noise in gene expression using thousands of designed sequences. Genome Res. 2014;24(10):1698–1706.
44. Landry CR, Lemos B, Rifkin SA, et al. Genetic properties influencing the evolvability of gene expression. Science. 2007;317(5834):118–121.
45. Tirosh I, Barkai N, Verstrepen KJ. Promoter architecture and the evolvability of gene expression. Journal of biology. 2009, 8(11):95.
46. Lehner B. Selection to minimise noise in living systems and its implications for the evolution of gene expression. Mol Syst Biol. 2008;4(1):170.
47. Lehner B. Conflict between noise and plasticity in yeast. Plos Genet. 2010;6(11):e1001185.
48. Dong D, Shao X, Deng N, et al. Gene expression variations are predictive for stochastic noise. Nucleic Acids Res. 2011;39(2):403–413.
49. Segal E, Widom J. Poly (dA: dT) tracts: major determinants of nucleosome organization. Curr Opin Struc Biol. 2009;19(1):65–71.

50. Jeffers TE, Lieb JD. Nucleosome fragility is associated with future transcriptional response to developmental cues and stress in C. elegans. Genome Res. 2017;27(1): 75–86.
51. Woo YH, Li W. Gene clustering pattern, promoter architecture, and gene expression stability in eukaryotic genomes. Proc Natl Acad Sci. 2011;108(8):3306–3311.
52. Shabalina SA, Ogurtsov AY, Spiridonov AN, et al. Distinct patterns of expression and evolution of intronless and intron-containing mammalian genes. Mol Biol Evol. 2010;27(8):1745–1749.
53. Dadiani M, van Dijk D, Segal B, et al. Two DNA-encoded strategies for increasing expression with opposing effects on promoter dynamics and transcriptional noise. Genome Res. 2013;23(6):966–976.
54. Cheng X, Hou Y, Nie Y, et al. Nucleosome positioning of intronless genes in the human genome. IEEE/ACM Transactions on Computational Biology and Bioinformatics. 2015; doi:10.1109/TCBB.2015.2476811
55. Lei L, Shi J, Chen J, et al. Ribosome profiling reveals dynamic translational landscape in maize seedlings under drought stress. Plant J. 2015;84(6):1206–1218.