# The dynamic epigenome

**The dynamic nature of functional information present in the genome—such as DNA methylation, histone modifications and chromatin organization—is beginning to be uncovered, along with the relationship between epigenomic patterning and developmental decisions or disease.**

Chromatin is a dynamic structure that must respond to myriad stimuli to regulate access to DNA. The epigenetic processes that modulate access to DNA in response to upstream signals include DNA methylation, covalent modification of histones, nucleosome remodeling, nuclear dynamics and chromatin interaction with regulatory noncoding RNAs. In recent years epigenetic processes have been extensively studied at a mechanistic level, but their dynamic nature in genomes is only beginning to be uncovered—thanks in part to herculean efforts by the Encyclopedia of DNA Elements (ENCODE) Consortium and others to generate hundreds of genome-wide datasets to map the human 'epigenome' and that of other organisms. Genome-wide studies are also being extended to analyze the relationship between epigenomic patterning and developmental decisions or disease, and the crosstalk between different epigenetic processes. In this issue, we present a special Focus on Epigenetic Dynamics (http://www.nature.com/nsmb/focus/epigeneticdynamics/) that explores emerging themes and the functional implications of epigenetic dynamics.

Nucleosomes represent the most basic level of chromatin organization, which has been likened to 'beads on a string' (an analogy that was the inspiration for the cover of this Focus issue). The covalent modification of histones is a vital means by which the cell modulates nucleosome mobility and turnover. As such, histone modifications are linked to essentially every cellular process requiring DNA access, including transcription, replication and repair. In their Review (p. 259), Zentner and Henikoff examine known properties of the major types of histone modification and the biological processes to which they are linked, and place the modifications in the context of nucleosome dynamics, whereby nucleosomes are translocated, unwrapped, evicted or replaced.

Nucleosome positioning is critical for transcription and other DNA-related processes, and nucleosomes occupy favored positions in the genome. In a Review dedicated to the late Jon Widom, whose work has been instrumental for this field, Segal and Struhl (p. 267) consider the mechanisms by which the genomic pattern of nucleosome positioning is achieved in yeast. They conclude that nucleosome positioning is not determined by any single factor but rather by the combined effects of several factors including DNA sequence, DNA-binding proteins, nucleosome remodelers and the transcription machinery.

The erasure and re-establishment of DNA methylation patterns during mammalian development is a classical example of epigenetic dynamics. Bergman and Cedar (p. 274) describe the dynamics of DNA methylation patterns during normal development *in vivo*, starting from fertilization through embryogenesis and postnatal growth, and the combination of sequence information and *trans*-acting factors that mediate the methylation and demethylation machinery.

Continuing with the theme of epigenetic control of developmental decisions, how complex genomes generate different cell types in a highly ordered and reproducible manner has intrigued geneticists and developmental biologists alike. We now know that epigenetic modifiers stabilize gene expression and ensure that patterns of DNA methylation and histone modifications are transmitted in cells as they divide to preserve cellular identity and lineage fidelity. Yet the epigenetic landscape undergoes extreme 'remodeling' at defined stages during mammalian development or as part of *in vitro* reprogramming strategies. Cantone and Fisher (p. 282) summarize recent advances in understanding how epigenetic remodeling contributes to cell-fate conversion *in vivo* and *in vitro*.

Although genomes and epigenomes have been characterized for many species, cell types and cellular conditions, the genome's three-dimensional organization and the importance of its topology for genomic functions such as transcription, replication and repair remain relatively poorly understood. However, new imaging technologies and genome-wide biochemical approaches, combined with functional data, are starting to reveal the significance of genome topology, as Cavalli and Misteli discuss (p. 290). This growing body of work will enable a better understanding of how genome organization influences gene function, and vice versa, and the role of this process in disease.

Last but not least, the discovery of noncoding RNAs has added an entire new level of complexity to our understanding of functional elements involved in gene regulation. Long noncoding RNAs (lncRNAs) have emerged as an abundant and functionally diverse group of regulatory RNAs that have been linked to the regulation of almost every stage of gene expression. Mercer and Mattick (p. 300) focus on the well-characterized ability for lncRNAs to function as epigenetic regulators. For example, many lncRNAs bind to chromatin-remodeling proteins and recruit their catalytic activity to specific sites, thereby modulating chromatin states and the epigenetic landscape. Considering these functional properties, combined with their abundance and diversity, lncRNAs potentially have a major role in epigenetic regulation.

Our knowledge of chromatin and epigenetic dynamics has moved well beyond the beads-on-a-string model, but there are plenty of outstanding questions that will challenge the field for years to come, and we look forward to seeing those developments on the pages of *NSMB*. If you would like to delve into the recent primary research papers that underpin the Review articles, we have collected relevant articles published in *NSMB* and *Nature* Research journals in a library (http://www.nature.com/nsmb/focus/epigeneticdynamics/library/). Finally, the Focus content will be freely available online for 3 months, thanks to generous support from Active Motif. ∎