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The past decade has seen a dramatic change in our perception of eukaryotic gene regulation and, this month, we feature two reviews that touch on some of the biological entities and processes that have led to this paradigm shift.

Not so long ago, the nucleosome was regarded as a static ‘packager of the genome’ — a banal octamer of histone proteins that hindered gene transcription. We now know that the covalent modification of these histone proteins is a dynamic process that impacts on chromatin structure, creating chromatin domains that are refractory or permissive to gene expression. And, as outlined by Kavitha Sarma and Danny Reinberg on page 139, variant histone subspecies also have important roles in the specification of specialized chromosome domains — such as centromeres and sites of transcriptional competence — as well as in crucial processes such as DNA repair and recombination.

The discovery of RNA interference (RNAi) in the late 1990s finally erased the perception of RNA as a mere intermediary in protein synthesis and ushered in an era of research into RNA-mediated gene regulation that has generated some of the most exciting advances in cell biology. The identification of the RNA-induced silencing complex (RISC) was an important milestone in the RNAi field and, on page 127, Erik Sontheimer reviews the composition, assembly and effector functions of RISC.

Interestingly, recent studies have linked the RNAi pathway to the assembly of heterochromatin and, as Sarma and Reinberg point out, the localization of the macroH2A histone variant to the mammalian inactive X chromosome relies on the presence of *Xist* RNA. The dissection of this complex interplay between histones and RNA promises to provide insights into the most fundamental aspects of nuclear biology.



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