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► **COVER:** 'Model organisms' by Patrick Morgan, inspired by the Perspective on p575.



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FROM THE EDITORS

This month's issue traces a path through epigenetic research from early observations of epigenetic phenomena, through the emergence of principles of gene regulation to the future application of epigenomics in human disease research.

The field of epigenetics owes much to studies of two classic phenomena: X-chromosome inactivation, which is discussed in a Review by Anton Wutz (p542), and genomic imprinting, which is the topic of a Perspective by Anne Ferguson-Smith (p565). Both are paradigms for epigenetic gene regulation, and their study, mainly in mice, underpins widely applied principles in this field. Wutz considers how stable silencing is achieved across an entire chromosome; the stepwise process that is emerging could be informative for other instances of gene silencing. However, X-chromosome inactivation also provides a lesson in caution when extrapolating across systems, as there are hints that inactivation occurs differently in other mammals.

Ferguson-Smith comments on the remarkable progress that has been made since the first use of the term 'imprinting' to the latest work on harnessing next-generation sequencing to seek new imprinted genes. Her historical Perspective also sets the stage for new horizons in epigenetics: characterizing epigenomes on a large scale and at high resolution and understanding genotype–epigenotype–phenotype relationships.

Also looking to the future, in a Review on p529, Stephan Beck and colleagues provide a framework for epigenome-wide association studies. Applying the principles of genome-wide association studies to variation in DNA methylation offers the exciting prospect of filling in some of the blanks in our understanding of common disease. This new direction highlights the fascinating recent transition from epigenetic phenomena being largely viewed as isolated curiosities to being seen as an integral part of complex traits.

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