EPIGENETICS

Intergenic transcription: more than just an onlooker

Despite strong suspicions that transcription through regulatory regions is key to the activation of certain genes, the evidence has always been circumstantial. Sabine Schmitt and colleagues now prove that just such a mechanism is required for the expression of a group of genes with important roles in development in *Drosophila melanogaster*, and is likely to be a widespread phenomenon.

Binding of Polycomb group (PcG) proteins to regulatory sequences known as Polycomb group response elements (PREs) leads to stable silencing of associated genes by maintaining chromatin in an inactive conformation. Reactivation takes place when trithorax group (trxG) proteins bind to the same sequences to reverse silencing. But how does switching between the two states occur? At the Bithorax complex of *D. melanogaster* — a cluster of genes that have essential roles in embryonic development — transcription of non-coding RNA from PREs has been shown by several groups to coincide with the silent-to-active transition. But is the production of these transcripts a consequence or a cause of reactivation?

To distinguish between these two possibilities, Schmitt and colleagues used transgenes that carried *Fab7*, a PRE-containing regulatory element of the Bithorax complex. They placed transcription through the *Fab7* PRE under the control of a constitutive *actin 5c* promoter and monitored the activation state of the PRE through the activity of a downstream marker gene that gives flies a red eye colour. All flies that carried the transgene expressed the marker, indicating an active chromatin conformation of *Fab7*. However, when the *actin 5c* sequences were excised from the transgene, expression of the marker was lost, providing strong evidence that transcription through the PRE is essential for its activation.

Are other PRE-controlled promoters regulated in the same way? The authors looked at the expression of non-coding RNAs produced from several other known or predicted PRE-containing regions, and found that they all showed similar expression patterns to the genes that are regulated by the PREs. So, although it remains to be confirmed, intergenic transcription might well be required in all these cases — and, by extension, at the many other genes that contain PREs.

Although this study demonstrates the importance of intergenic transcription in the switch from inactive to active chromatin, two important questions remain to be answered. First, how does transcription reverse the silent state? And second, what triggers transcription through promoter regions in areas of inactive chromatin in the first place?

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References and links

ORIGINAL RESEARCH PAPER
Schmitt, S., Prestel, M. & Paro, R. Intergenic transcription through a Polycomb group response element counteracts silencing. *Genes Dev.* 25 February 2005 (doi:10.1101/gad.326205)

WEB SITE
The Centre for Molecular Biology at the University of Heidelberg: http://www.zmbh.uni-heidelberg.de

IN BRIEF

RNA WORLD

A potential role for RNA interference in controlling the activity of the human LINE-1 retrotransposon.

Soifer, H. S. *et al. Nucleic Acids Res.* **33**, 846–856 (2005)

Vigilins bind to promiscuously A-to-I-edited RNAs and are involved in the formation of heterochromatin.

Wang, Q. *et al. Curr. Biol.* **15**, 384–391 (2005)

These papers provide new insights into cellular responses to double-stranded RNA (dsRNA). LINE-1 elements pose a threat to genome integrity in human cells through their ability to move around by retrotransposition. Soifer *et al.* present the first evidence that LINE-1 dsRNAs are targets of the RNAi machinery, indicating that this pathway is one form of defence that the human genome uses against retrotransposition. dsRNAs from various sources also undergo promiscuous adenosine-to-inosine editing, and Wang *et al.* provide evidence that this leads to the formation of silent heterochromatin at the corresponding genomic sequences. RNAi and RNA editing therefore provide alternative and perhaps overlapping pathways to RNA-mediated silencing.

TECHNOLOGY

MAGIC, an *in vivo* genetic method for the rapid construction of recombinant DNA molecules.

Li, M. Z. & Elledge, S. J. *Nature Genet.* **37**, 311–119 (2005)

Conventional cloning is an expensive and time-consuming process that involves multiple steps from the initial DNA plasmid preparation to transformation. The need to achieve high-throughput recombinant-DNA production led Li and Elledge to design a new cloning method that involves only three steps. The approach relies on bacterial conjugation, *in vivo* site-specific endonuclease cleavage and homologous recombination to place the DNA fragment of interest under the control of new regulatory elements in the desired vector. It's cheap and easy — it's MAGIC.

TECHNOLOGY

Ubiquitous GFP expression in transgenic chickens using a lentiviral vector.

Chapman, S. C. *et al. Development* **132**, 935–940 (2005)

Production of transgenic chickens is an attractive goal for both pharmaceutical and developmental biologists, but has been held back owing to technical challenges. Chapman and colleagues now show that ubiquitous GFP expression in the chicken embryo can be achieved using a lentiviral vector. With the chicken genome sequence now available, this method will be useful for investigating gene expression during embryonic development — an important tool given that the chicken is an established developmental model. It also provides a model for a new generation of transgenics for studying the expression of pharmaceutical products in egg albumen.

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