Nature Reviews Genetics | AOP, published online 9 May 2006; doi:10.1038/nrg1873

DEVELOPMENT

A developing role for Polycomb proteins

DOI:
10.1038/nrg1873

URLs
Research highlight
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Polycomb group (PcG) proteins have essential roles in differentiation, allowing cells to memorize the transcriptional responses of genes to transient developmental signals. A slew of recent papers now reveal many new targets for PcG proteins and add to the emerging evidence that they have dynamic roles during development. As described in an accompanying Research Highlight, these aspects of PcG function also turn out be central to the properties of stem cells.

Two studies — from Tolhuis and colleagues and Bracken and colleagues — looked at the role of PcG proteins in cell lines (*Drosophila melanogaster* and human, respectively) that are no longer pluripotent, but are not terminally differentiated. A third study, from Nègre *et al.*, examined PcG functions during fly development. All three used genomic profiling methods to generate unbiased pictures of how PcG protein binding is distributed, either across the whole genome or in large chromosomal regions.

In each case, a wealth of new target genes for PcG proteins was revealed. As might be expected, a large proportion of these encode transcriptional regulators or signalling proteins with developmental functions, in line with known PcG targets. However, intriguing new roles of PcG proteins were also highlighted. For example, Tolhuis and colleagues identified several genes with roles in steroid hormone biosynthesis, suggesting a potential function for PcGs in fly metamorphosis.

PcG proteins maintain transcriptional silence in a process that is thought to involve trimethylation of histone H3 at Lys27 (H3-K27). Consistent with this, Tolhuis *et al.* and Bracken *et al.* found that PcG binding generally correlated with this epigenetic mark, and with low levels or absence of transcription.

However, PcG proteins seem to have a more dynamic role than simply binding and remaining at their target sites. Nègre *et al.* found that the profile of PcG binding changes as *Drosophila* development progresses, and that although a particular gene might be a PcG target, this is not necessarily the case in all tissues or developmental stages. In line with this, Bracken *et al.* showed that the displacement of PcG proteins is important for differentiation: the increased expression of target genes in response to a differentiation-inducing stimulus corresponded with a decrease in PcG binding.

Two further studies, which are discussed in the accompanying Research Highlight, reveal that this dynamic regulation is also important in embryonic stem cells. They describe how PcG proteins keep differentiation-specific genes in a state that is transcriptionally silent and yet poised for activation when expression is needed — seemingly a common theme in the role of PcG proteins throughout development.

These studies hint at many roles of PcG proteins in development and differentiation that have yet to be investigated in detail. Exploring how these proteins interact with other chromatin components, and how they are regulated by developmental cues, will be key to our understanding of how transcriptional states are memorized and modified as cells progress towards their ultimate fates.

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ORIGINAL RESEARCH PAPERS Tolhuis, B. *et al.* Genome-wide profiling of PRC1 and PRC2 Polycomb chromatin binding in *Drosophila melanogaster*. *Nature Genet.* 20 April 2006 (doi:10.1038/ng1792) | Nègre, N. *et al.* Chromosomal distribution of PcG proteins during *Drosophila* development. *PLoS Biol.* **4**, e170 (2006) | Bracken, A. P. *et al.* Genome-wide mapping of Polycomb target genes unravels their roles in cell fate transitions. *Genes Dev.* 17 April 2006 (doi:10.1101.gad.381706)