GENE REGULATION

Sequence, chromatin, action!

When a cell receives a signal that alters its transcriptional programme, primary response genes (PRGs) are rapidly induced. Two recent papers provide new insights into the basis of the speedy activation of mammalian PRGs.

Although some mammalian PRGs depend on chromatin remodelling by SWI–SNF complexes for inducible expression, others do not. By studying PRGs that are induced by Toll-like receptor 4 (TLR4) signalling in mouse macrophages, Ramirez-Carrozzi *et al.* determined that dependency on SWI–SNF remodelling is correlated with the absence of a CpG island in the promoter. Even in unstimulated cells, the promoters of TLR4-responsive genes that contain a CpG island had features of constitutively active chromatin; furthermore, CpG islands were assembled into chromatin with reduced nucleosome stability *in vitro*. The authors propose that the presence of a CpG island, in combination with binding of constitutively expressed transcription factors, results in active chromatin, explaining how these genes can be induced without SWI–SNF remodelling. These PRGs are generally inducible by a wide range of stimuli, whereas those that require remodelling are more specifically activated. Ramirez-Carrozzi *et al.* propose that independence from SWI–SNF complexes is key to the more promiscuous activation of CpG-containing promoters.

In a second study, Hargreaves and colleagues focused on pre-association of RNA polymerase II (RNAPII) with promoters, a phenomenon that has been proposed to poise genes for expression. Also looking at TLR4 signalling, the authors identified a set of rapidly responding PRGs at which RNAPII binding and active histone marks are seen in the absence of induction. However, contrary to what has been observed for *Drosophila melanogaster* genes, RNAPII is not paused at the initiation stage. Instead, full-length unspliced transcripts are produced, and regulation occurs at the level of mRNA elongation and processing. The authors provide evidence that the presence of a corepressor at these genes prevents productive transcription in the absence of TLR4 signalling, and that it is the acetylation of histones at specific residues in response to induction that provides the rapid switch to corepressor removal and production of mature transcripts. Consistent with the Ramirez-Carrozzi *et al.* study, these rapidly responding PRGs tend to have high CG levels in their promoters.

These studies make important steps towards understanding how sequence and chromatin features of genes relate to the dynamics of gene expression. Future studies that look at responses to a wider range of stimuli and at genes with different expression dynamics will add further detail to this picture.

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ORIGINAL RESEARCH PAPERS
Ramirez-Carrozzi, V. R. *et al.* A unifying model for the selective regulation of inducible transcription by CpG islands and nucleosome remodeling. *Cell* **138**, 114–128 (2009) | Hargreaves, D. C. *et al.* Control of inducible gene expression by signal-dependent transcriptional elongation. *Cell* **138**, 129–145 (2009)