EPIGENETICS

Transcriptional memory remodelled

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10.1038/nrg2110

URLs

Entrez
 GAL1
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&md=Retrieve&dopt=full_report&list_uids=852308

SWI2

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&md=Retrieve&dopt=full_report&list_uids=854465

Craig Peterson's web site:
<http://www.umassmed.edu/pmm/faculty/peterson.cfm>

For cells to respond effectively to their environment, forming a 'memory' of transcriptional responses to certain conditions can be a useful strategy. It is generally believed that histone modifications have a role in this type of mechanism. Now, work in yeast reveals that ATP-dependent chromatin remodelling enzymes provide a second form of epigenetic transcriptional memory.

The *Saccharomyces cerevisiae* **GAL1** gene product allows cells to use galactose as an energy source. Kundu and colleagues found that when cells are first exposed to galactose, **GAL1** expression takes more than an hour to reach its peak. However, if cells are grown in the presence of galactose, followed by repression of **GAL1** expression by glucose and then re-exposure to galactose, transcription

at the **GAL1** locus resumes rapidly, peaking in less than 10 minutes. The authors propose that yeast cells remember their initial encounter with galactose and can somehow reactivate **GAL1** expression more quickly. This response is maintained through at least one cell division, suggesting that a form of epigenetically inherited transcriptional memory is at work.

By tracking protein recruitment at **GAL1**, the authors ruled out the possibility that components of the transcriptional machinery are responsible for this epigenetic memory. They also eliminated roles for several histone-modifying enzymes that might be considered as likely candidates for mediating the memory: deletions of the genes encoding these proteins had no effect on the re-induction of **GAL1**.

Instead, the authors found that the **SWI2** gene, which encodes the SWI/SNF ATP-dependent remodelling enzyme, was involved. Deletion of this gene has no effect on steady-state **GAL1** expression, but abolishes the rapid re-induction of **GAL1** after a second exposure. This effect is not simply due to a general need for SWI/SNF in antagonizing glucose repression, as **GAL1** transcripts are eventually made in *swi2Δ* mutants. Kundu and colleagues propose that SWI/SNF is needed after initial **GAL1** transcription to establish a heritable epigenetic state that allows rapid reinduction. Using a strain carrying a mutation in the ATPase domain, they showed that the enzymatic activity of SWI/SNF is essential for establishing this state.

Previous studies have shown that an ATP-dependent remodeller of the ISWI family — members of which are generally associated with transcriptional repression — is recruited to **GAL1** during transcriptional induction. When the *swi2Δ* mutation was combined with deletions of either of the *S. cerevisiae* genes that encode ISWI-like enzymes, rapid **GAL1** re-induction was abolished. On this basis, the authors propose a model in which SWI/SNF is needed to prevent an ISWI-mediated return of chromatin at **GAL1** to a transcriptionally repressive state.

ISWI-like enzymes and SWI/SNF are already known to have antagonistic effects at several other genes. Future investigations at these and other loci should reveal whether transcriptional memory involving ATP-dependent remodelling is a widespread phenomenon in yeast and other organisms.

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ORIGINAL RESEARCH PAPER Kundu, S., Horn, P.J. & Peterson, C.L. SWI/SNF is required for transcriptional memory at the yeast **GAL** gene cluster. *Genes Dev.* **21**, 997–1004 (2007)

WEB SITE

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