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GENE REGULATION

Transcription factor clutch control

The spatio-temporal expression of genes is influenced by transcription factor binding to DNA regulatory sequences. Chromatin immunopreciptation assays are frequently used to provide a 'snapshot' of this binding. Using an extension of this technique that can assess binding kinetics genome-wide, a recent study has revealed important insights into transcription factor binding dynamics in relation to gene expression.

The authors explored transcription factor binding dynamics in yeast cells that had been modified to set up a controlled competition between two versions of the same transcription factor: Rap1. Two versions of Rap1, Rap1–Flag and Rap1–Myc, were controlled by different promoters, such that Rap1–Flag was continuously expressed, whereas Rap1–Myc was experimentally inducible. By measuring the binding of the Rap1 variants over time after Rap1–Myc induction, the authors found that in some locations Rap1–Myc rapidly out-competed Rap1–Flag, but in other locations Rap1–Myc was incorporated much more slowly. This indicates differences in the binding dynamics of Rap1 at different locations across the genome.

Genes with a slower Rap1 turnover had higher levels of transcription than those with a faster Rap1 turnover. Interestingly, the sites with a fast Rap1 turnover have also been previously reported to have fast rates of nucleosome exchange. The authors suggest that a continual turnover, or 'treadmilling', of transcription factors and nucleosomes can poise a site for transcriptional activation. In this model, when the histone affinity to DNA is lowered (possibly by chromatin-remodelling enzymes, modification of histones or incorporation of a histone variant) the transcription factor can quickly achieve stable binding to the target site, thereby activating transcription. The authors propose that this dynamic treadmilling mechanism could allow a rapid, molecular, 'clutch-like' genomic response to development and environmental changes.

> "turnover…of transcription factors and nucleosomes can poise a site for transcriptional activation"

According to the authors' data, the dynamics of transcription factor binding are more closely correlated to gene expression levels than to transcription factor occupancy, highlighting the importance of considering binding turnover dynamics in future studies.

Bryony Jones

ORIGINAL RESEARCH PAPER Lickwar, C. R *et al.* Genome-wide protein–DNA binding dynamics suggest a molecular clutch for transcription factor function. *Nature* **484**, 251–255 (2012)

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