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Research highlights

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Chromatin determines transcription factor binding

For most transcription factors, only a fraction of potential binding sites is occupied by the protein at any given time. What accounts for this selectivity is largely unknown. John *et al.* demonstrate in genome-wide experiments that the binding behavior of a glucocorticoid receptor is determined largely by chromatin structure. They investigate the relationship between the binding sites of the receptor after hormone stimulation with the pre-existing patterns of chromatin accessibility in two cell types. Their comparison of ChIP-seq data with analysis of DNA accessibility by digital DNase I profiling reveals that up to 95% of the binding occurred at sites with an open chromatin formation. The dominant effect of chromatin structure can be modulated by the specific glucocorticoid receptor binding element present, as some motifs are more likely to be bound even if the DNA is inaccessible to DNase I, and by nearby binding sites of additional co-regulatory factors, such as AP-1. As glucocorticoids are widely used to combat inflammatory, autoimmune and allergic conditions, the study raises the intriguing possibility that patient responses to nuclear receptor ligand drugs might be stratified on the basis of epigenetic status (*Nat. Genet.* published online, doi:10.1038/ng.759, 23 January 2011) *ME*

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