

Nonspecific Protein-DNA Binding Is Widespread in the Yeast Genome

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Recent genome-wide measurements of binding preferences of ~200 transcription regulators in the vicinity of transcription start sites in yeast, have provided a unique insight into the cis- regulatory code of a eukaryotic genome (Venters et al., Mol. Cell 41, 480 (2011)). Here, we show that nonspecific transcription factor (TF)-DNA binding significantly influences binding preferences of the majority of transcription regulators in promoter regions of the yeast genome. We show that promoters of SAGA-dominated and TFIID-dominated genes can be statistically distinguished based on the landscape of nonspecific protein-DNA binding free energy. In particular, we predict that promoters of SAGA-dominated genes possess wider regions of reduced free energy compared to promoters of TFIID-dominated genes. We also show that specific and nonspecific TF-DNA binding are functionally linked and cooperatively influence gene expression in yeast. Our results suggest that nonspecific TF-DNA binding is intrinsically encoded into the yeast genome, and it may play a more important role in transcriptional regulation than previously thought.

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