

## **Bioinformatics Approaches to Model *cis*-Regulatory Modules and Putative Transcription Factor Partners**

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The combinatorial theory of gene regulation by transcription factors (TFs) states that TFs act cooperatively to mediate target gene activation or repression. All signal transduction pathways converge at the level of gene expression where positive and negative modulators of transcription delineate the pattern of gene expression. Consequently, modeling and elucidating the combinatorial interaction of TFs and corresponding *cis*-regulatory logic in target promoters is of paramount interest.

Recently, by combining a systematic computational approach and ChIP-chip method, we performed genome-wide identification of TF target genes (Jin, et al. *Nucleic Acids Res.* 32: 6627-6635; Cheng et al. *Molecular Cell*, 2006 23:393-404). The integrative approach involves comparative genomics, using promoters of orthologous mammalian genes (Palaniswamy et al. *Bioinformatics*, 21:835-836), ChIP-chip experiments and statistical data mining. Using ChIP-chip experiments and correlating acetylation and dimethylation at H3-K9 with gene activation and repression, respectively, we classified the responsive promoters into acetylated and methylated groups. Computational modeling using classification and regression tree (CART) allowed us to distinguish *cis*-regulatory modules among these responsive promoters and identify putative TF partners.

As an application of this method, I will discuss the bioinformatics approaches to interrogate combinatorial control of ER $\alpha$ -regulated transcription, a strategy that can be used to examine additional TF modules.