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Context-specific Combinatorial Interaction of Transcription Factors in Gene Regulation

It is well known that transcription factors (TFs) form complexes with other TFs or cofactors to assert transcriptional regulation of genes. However, it is the first time that a series of high-throughput experiments have been performed to identify the binding sites of more than a hundred TFs in ~70 different cell-types, as part of the ENCODE project. This gave us the unique opportunity to address one of the central themes of gene regulation, i.e., combinatorial interaction among the TFs. Expression profiles, DNase1 hypersensitive sites, nucleosome depleted sites and histone modification data were also available across the entire genome. This enabled the cross-comparison and made integration feasible and robust. Here we describe our findings based on ~100 TFs across five cell lines. We describe the context-specificity of specific combinations of TF-TF interactions. How these combinations can yield varying outputs, in terms of gene regulation and functional modularity will be discussed.