In addition to differences in the coding regions of a genomic sequence, the elements responsible for the regulation of gene transcription have a major impact on the phenotype. New methods, both experimental and computational, for the study of transcription regulation are constantly emerging. One of these new methods is chromatin immunoprecipitation, or ChIP-chip, which allows for the genome-wide discovery of transcription factor binding sites using microarrays. The combination of such experimental methods with computational sequence-based predictive analyses generally increases the specificity of transcription factor binding site detection.

In this study, an analysis of a ChIP-chip data set comprising the transcription factors ATF-2 and c-Jun is performed using two different ranking methods, along with a Monte Carlo type false discovery rate estimation. This analysis is combined with an in silico analysis predicting specific ATF-2 binding sites in the obtained promoter sequences, complemented by phylogenetic footprinting, which is a study of the evolutionary conservation of the predicted sites.

The results from the analysis are inconclusive in that the results of the sequence analyses do not support those obtained from the ChIP-chip analysis in a way that was expected based on literature. It is evident that the observations made in this study are specific to the transcription factor, microarrays and binding site model used, and it is impossible to conclude that the combination of ChIP-chip and in silico site prediction would not be useful in general. Phylogenetic footprinting is clearly observed to limit the number of predicted binding sites considerably, and it is evident that the sites retained after phylogenetic footprinting are generally highly conserved.

It is clear that the quality of ChIP-chip microarrays and their analysis methods will improve in the future, as will the sequence-based prediction methods, which rely on experimentally derived information on the binding tendencies of transcription factors. This development will hopefully increase the potential of analyses such as the one presented here.

Keywords: ChIP-chip, sequence analysis, gene regulation, transcription factors