Placing transcription factor complexes into gene regulatory networks

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Interactions between transcription factors and DNA are important for gene transcriptional regulation. Cooperativity amongst TFs can lead to improvement in DNA binding specificities. Recent studies show that cooperative binding events are evolutionarily conserved and show more effects on gene transcription than single TFs. A gene regulatory network, built with TF complexes showing significant cooperativity as regulatory drivers, can be helpful for mechanistic understanding of transcriptional regulation and may have predictive value for diseases like cancer. Main aim of this work is to develop an automated pipeline to map putative transcription factor complexes onto gene regulatory networks. We consider the raw RNA-seq data of two groups of monocytes - classical and non-classical. We compare the differential complexes obtained from the stand-alone software CompleXchange[1] and TF-gene interactions predicted by, our in-house web server, TFmiR2[2] to extract common TFs and target genes. We use the tool Fimo[3] from the MEME suite to scan the TF motifs in the promoter regions of their common genes and are subjected to constraints to filter out non-essential complexes. Cytoscape[4] is used to visualize the initial network. Our results indicate that many of the individual TFs targeting common genes in the regulatory network are part of protein complexes.

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