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Type	Poster
Session	Biological Databases
Title	Exploring functionally annotated transcriptional consensus regulatory elements with CONREL
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Motivation

Cis-regulatory elements are genomic regions of DNA that concur to the regulation of the transcription of nearby genes. Transcription factors (TFs) are key cellular components that orchestrate gene expression. Understanding the interaction between human genome regulatory elements and transcription factors is fundamental to elucidate the structure of gene regulatory networks. We present CONREL, a web application that enables the exploration of annotated regulatory elements across the human genome.

Methods

Regulatory elements are built using a ‘consensus’ approach by computing the agreement of histone mark annotations across multiple experiments. Specifically, ENCODE ChIP-seq peak data was downloaded for all cell lines with H3K4me1, H3K4me3 or H3K27ac histone markers peak data available considering both narrowPeak and broadPeak datasets. For each marker, peak regions were merged for sample replicates and then for different experiments of the same cell line. Consensus regions for promoters were defined considering all the regions occupied by H3K4me3, within a window of 1Kbp around a Transcription Start Site (TSS). Consensus regions for enhancers were defined considering regions occupied by H3K4me1, depleted of H3K4me3, and with distance greater than 1Kbp from TSS. Enhancer regions were considered active if overlapped by at least one H3K27ac peak region. Finally, tissue-specific consensuses were computed by merging consensus regions across cell lines that originated from the same tissue, while global consensuses were computed by merging consensus regions across all cell lines.
The Total Binding Affinity describes the affinity of a DNA sequence for a TF described by a Positional Frequency Matrix (PFM) with a single score, the method takes into account binding sites of all possible affinities, and weighting them based on a physical model of TF:DNA interactions. TBA scores were computed for all TF PFMs across all tissue-specific and global CREs. A TBA score was computed considering the CRE sequence described by the human reference genome (hg19) and a set of TBA scores were computed on all common alleles identified from 1000 Genomes Project individuals.

Results

We developed CONREL, a web application that provides an extensive collection of consensus promoters, enhancers and active enhancers available for 198 cell-lines across 38 tissue types, and also combined to provide global consensuses. In addition, CONREL provides collections of TFs that show enriched TBAs at different significance thresholds and can hence be used to elucidate regulatory mechanisms at specific regions. In addition, the landscape of TF TBA enrichment frequencies across common alleles in 1000 Genomes Project individuals is also provided for each regulatory element, allowing to identify TFs that might play a role in transcripts regulation only in a fraction of individuals and/or in an allele-specific manner. The resource is freely available at https://bcglab.cibio.unitn.it/conrel

Info

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Figure

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Availability	-

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