

Poster H-6

Regulatory Content of Vertebrate Enhancers



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Short Abstract: Long-range developmental enhancers in vertebrate genomes often coincide with highly conserved non-coding regions. We have devised a graph-based approach to discover regulatory information in such elements, and applied it to a collection of experimentally characterized enhancers to assign their expression patterns to specific motifs or combinations thereof.

Long Abstract:

About 98% of the human genome does not correspond to protein coding regions (1). In the non-coding part of the genome there are thousands of highly conserved noncoding regions (2-4) which show significant level of conservation across all vertebrates. Recent studies have demonstrated evidence that many of such conserved regions function as distal regulatory elements and cluster around transcription factor and developmental genes (2,3), function as enhancers (4,5) and that their long-range activity is preferentially (6) captured by an retroviral enhancer trap cassettes in zebrafish. While their level and extent of conservation are hard to explain solely by the need to maintain transcription factor binding properties, it is reasonable to assume that they contain regulatory information that mediates their effect on target genes.

In this work, we aim to extract the regulatory information from long-range enhancers by finding motifs and their combinations associated with their distinct expression domains. Several sets of enhancer sequences are annotated with their experimentally determined expression pattern and searched for motifs they share in the same way as they do their expression patterns. We have developed a statistical sampling approach to estimate statistical significance of co-occurrence of motifs across different enhancers. We show preliminary evidence that this method can be applied to general gene clusters for the discovery of new regulatory patterns in HCNRs even in the absence of their individual experimental characterization.

References

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