Global prediction of gene regulatory landscape using gene expression

We evaluate the feasibility of using a biological sample's transcriptome to predict its genome-wide regulatory element activities measured by DNase I hypersensitivity (DH). We develop BIRD, Big Data Regression for predicting DH, to handle this high-dimensional problem. Applying BIRD to the Encyclopedia of DNA Elements (ENCODE) data, we found that to a large extent gene expression predicts DH, and information useful for prediction is contained in the whole transcriptome rather than limited to a regulatory element's neighboring genes. We show applications of BIRD-predicted DH in predicting transcription factor-binding sites (TFBSs), turning publicly available gene expression samples in Gene Expression Omnibus (GEO) into a regulome database, predicting differential regulatory element activities, and predicting regulatory landscape of single cells and samples with small number of cells. Besides improving our understanding of the regulome-transcriptome relationship, this study suggests that transcriptome-based prediction can provide a useful new approach for regulome mapping.

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Thursday August 23, 2018
3:30 pm - 4:30 pm
Blue Cross and Blue Shield of North Carolina Foundation Auditorium