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Correlated transcription modules uncovered by high-precision single-cell transcriptomics

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Single cell transcriptome sequencing has provided a wealth of data about differential expression across cell types and conditions. However, such data are of limited utility for inferring regulatory relationships between genes because multiple regulatory pathways and their downstream targets are up- or down-regulated in unison. Here, we generate more specific and functionally enriched modules by clustering genes according to correlations in steady-state expression fluctuations. We developed a novel single-cell RNA-seq method called MALBAC-DT to measure these correlations in homogenous cell populations and found numerous intercorrelated gene clusters with cell-type specific functional enrichments. Literature analysis and RNAi knockdown of the TP53 transcription factor confirmed that a 50-gene module enriched for p53 signaling consisted almost entirely of direct TP53 targets. This approach provides a powerful way to advance our functional understanding of the genome.

Biography

Alec Chapman is a postdoctoral researcher in the lab of Sunney Xie at Harvard University. His work has focused on developing new methods for single cell genome and transcriptome sequencing and applying these methods to study biological systems ranging from development to cancer. He is interested in regulation of gene expression and how cells make decisions in the presence of noise. He received his Ph.D. from Harvard University and did his undergraduate work at Princeton University.

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