Systematic identification of gene family regulators in mouse and human embryonic stem cells.

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Abstract:

Pluripotent self-renewing embryonic stem cells (ESCs) have been the focus of a growing number of high-throughput experiments, revealing the genome-wide locations of hundreds of transcription factors and histone modifications. While most of these datasets were used in a specific context, all datasets combined offer a comprehensive view of chromatin characteristics and regulatory elements that govern cell states. Here, using hundreds of datasets in ESCs, we generated colocalization maps of chromatin proteins and modifications, and built a discovery pipeline for regulatory proteins of gene families. By comparing genome-wide binding data with over-expression and knockdown analysis of hundreds of genes, we discovered that the pluripotency-related factor NR5A2 separates mitochondrial from cytosolic ribosomal genes, regulating their expression. We further show that genes with a common chromatin profile are enriched for distinct Gene Ontology (GO) categories. Our approach can be generalized to reveal common regulators of any gene group; discover novel gene families, and identify common genomic elements based on shared chromatin features.

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