Genome-wide 3D maps of regulatory interactions in the mouse developing forebrain

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Studying the role of genome packaging in gene regulation

Existing methods for mapping 3D genome interactions:
- FISH - limited in throughput and resolution.
- Hi-C - regulatory interactions are often obscured among many non-functional DNA-DNA interactions.

ChIA-PET

- ChIA-PET - experimental way of measuring genome-wide DNA-DNA interaction mediated by protein of interest.

Data parsing and mapping

- ChIA-PET of RNA PolII and H3K27ac in mouse brain E16.5
- Goal: Genome-wide identification of regulatory interactions in the mouse developing forebrain

- Input: 498 million 150bp paired-end reads.
- Distribution of "half" lengths
  - 5.9% 20bp
  - 45% All reads

Comparison to standard Mmel (20bp long) ChIA-PET

Most interactions are within TADs (94%)

Obtaining a high-confidence set of interactions

1. Filter out:
   - Interactions between different chromosomes
   - Self-igation interactions (dist<1200 bp and same strand)
   - Long-range interactions (dist>1Mbp)
2. Use the in vivo binding landscape of PolII, CBP, and the H3K27ac to prune our set of interactions:

Peak set: peaks from ChIP-Seq experiments of PolII, H3K27ac and CBP from mouse brain E16.5 (~90,000 peaks)
Retain only iPETs = same-chromosome peak-to-peak interactions.

Interactions enriched for enhancer-promoter and promoter-promoter interactions

In total, we found in our data ~1,000 promoters which interact (#iPETs>2) with regulatory regions (enhancers/silencers).

In vivo enhancer assay

Identifying Genome-Wide Enhancer Candidates

References


Other