Transcriptional Interactome in Mouse Genome

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The work conducted by the DOE Joint Genome Institute is supported by the Office of Science of the U.S. Department of Energy under Contract No. DE-AC02-05CH11231

Abstract
Distant regulatory elements have been shown to influence gene function via long-range chromatin interactions. In this study, we depict the dynamic transcriptional interactomes mediated by RNA polymerase II (RNAPII) with the newly developed Chromatin Interaction Analysis by Pair End diTag (ChIA-PET) to define the chromatin organizations pertinent to transcription regulation and epigenetic control in pluripotent embryonic stem cells (mES), neural stem cells (mNS) and neurosphere cells (mNP). With over 150 million ChIA-PET sequencing, thousands of cis- and trans- chromatin interactions tethered by RNAPII are defined. We plan to integrate the transcription interactome maps with global transcription expression changes, promoter activities, gene activities and major epigenomic features to define spatial distribution and temporal regulation of transcription networks.

I. Project goal

1. CHIA-PET sequencing and mapping summary

<table>
<thead>
<tr>
<th>Total PETS</th>
<th>160.1M</th>
<th>152.2M</th>
<th>146.7M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unique mapped PETS</td>
<td>94.0M (58.8%)</td>
<td>72.1M (47.0%)</td>
<td>79.7M (47.9%)</td>
</tr>
<tr>
<td>Merged Unique PETS (12bp)</td>
<td>66.4M (41.6%)</td>
<td>38.7M (25.4%)</td>
<td>8.1M (4.9%)</td>
</tr>
<tr>
<td>Self-aligation PETS</td>
<td>26.9M (40.3%)</td>
<td>5.6M (14.3%)</td>
<td>721K (8.9%)</td>
</tr>
<tr>
<td>Binding Sites</td>
<td>24,201</td>
<td>34,867</td>
<td>11,819</td>
</tr>
<tr>
<td>Inter-chromosomal PETS</td>
<td>3.0M (4.5%)</td>
<td>2.1M (5.5%)</td>
<td>765K (9.4%)</td>
</tr>
<tr>
<td>Inter-chromosomal Interactions (2+)</td>
<td>27,656</td>
<td>59,152</td>
<td>1,700</td>
</tr>
</tbody>
</table>

2. Evaluation noise level via chimera library

Ongoing works
1. Validation our dataset via various experiments, such as 3C, FISH
2. Integrating with other genomic datasets, CHIP-Seq, RNA-Seq, RIP-Seq, methylome
3. Dynamic interactome analysis across the mouse genome
4. Modeling the 3-D gene regulation networks

References
Fullwood. M et al., Nature 462, 58-64, 2009
Li. G et. al., Genome Biology, 11(2):R22, 2010
Handoko. L et. al., Nature Genetics 43, 630-638, 2011