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The development of Nano-C allows the characterization of TAD boundaries with unprecedented resolution

Chromosome conformation capture (3C) methods are a powerful tool for uncovering 3D genome organization. Short-read Illumina sequencing restricts 3C to the description of average conformations within large cell populations. Significant variation between individual cells within the same population may be present though. For instance, if different contacts happen simultaneously, exclusively, or in subsets, cannot be discerned by methods based on population-level pairwise contacts.

In my project, I aim to determine the degree of cellular heterogeneity of TAD (Topologically Associating Domain) boundaries. TADs are separated by boundaries that are often bound by the CTCF insulator protein. Several recent studies have reported that CTCF often binds at multiple sites around TAD boundaries (e.g. Madani Tonekaboni et al, 2019). We have recently reported that many TAD boundaries provide a more gradual insulation, suggesting they act like 'transition zones'(Chang et al, 2020). Considering the dynamic nature of CTCF binding to the DNA (Hansen et al, 2017), clustering of CTCF binding at boundaries may thus stabilize the insulation of neighboring TADs.

To measure the variable nature of TAD boundaries, I have developed "Nano-C", a PCR-free multi-contact assay that combines 3C with Nanopore sequencing, to identify multiple interactions from defined genomic loci in single cells. Using Nano-C, I have confirmed that individual CTCF binding sites contribute additively to TAD boundary function in individual cells. Moreover, I have found that this cell-to-cell variation contributes to the insulation-strength of different TAD boundaries. These results support the notion that clustering of CTCF binding at boundaries provides redundancy to stabilize TAD structure and gene regulatory function.

References:

Chang, L.-H., Ghosh, S. & Noordermeer, D. TADs and Their Borders: Free Movement or Building a Wall? *J Mol Biol* **432**, 643-652 (2020).

Hansen, A. S., Pustova, I., Cattoglio, C., Tjian, R. & Darzacq, X. CTCF and cohesin regulate chromatin loop stability with distinct dynamics. *Elife* **6** (2017).

Madani Tonekaboni, S. A., Mazrooei, P., Kofia, V., Haibe-Kains, B. & Lupien, M. Identifying clusters of cis-regulatory elements underpinning TAD structures and lineage-specific regulatory networks. *Genome Res* **29**, 1733-1743, (2019).

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