Cleveland Clinic Innovations

PRODUCT
Software for analyzing 3D chromatin organization

INDICATION
- Chromatin loop detection
- Chromatin interaction analysis

VALUE PROPOSITION
- High sensitivity, accuracy, and reproducibility
- Superior resolution (10Kb)
- Cell type-specificity

DEVELOPMENT STAGE
Software has been built and validated

RELATED PUBLICATIONS

Hu M, et al. (2019). MAPS: model-based analysis of long-range chromatin interactions from PLAC-Seq and HiChIP experiments. PLOS Computational Biology. 15(4):e1006982.

Hu M, et al (2023). SnapFISH: a computational pipeline to identify chromatin loops from multiplexed DNA FISH data. Nature Communications. 14, Article number: 4873.

Hu M, et al (2023). SnapHiC-D: a computational pipeline to identify differential chromatin contacts from single cell Hi-C data. Briefings in Bioinformatics. 24(5):bbad315.

Hu M, et al (2021). SnapHiC: a computational pipeline to identify chromatin loops from single cell Hi-C data. Nature Methods.18(9):1056-1059.

CONTACT INFORMATION

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Computational Models to Identify Chromatin Loops and Interactions

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UNMET NEED
Growing evidence supports an important role of chromatin spatial organization in genome function and delineates its alterations as prominent causes of disease including cancer. Chromatin loops and interactions are key structural features of chromatin spatial organization and serve as the structural basis of gene regulation. Existing methods to characterize the spatial organization of chromatin suffer from suboptimal performance. There is a need for computational tools that can detect chromatin loops and analyze chromatin interactions with high sensitivity, reproducibility, accuracy, and resolution from different input datasets generated by diverse chromatin architecture mapping technologies in a cell specific manner.

SOLUTION
Cleveland Clinic investigator has developed superior computational approaches to speed up the analysis of chromatin spatial organization.

- MAPS, Model-based Analysis of PLAC-seq and HiChIP, to process data from PLAC-seq and HiChIP experiments and identify long-range chromatin interactions. MAPS shows superior performance (sensitivity, reproducibility, accuracy, resolution) over existing software tools and can identify a large number of biologically relevant chromatin interactions that are missed by state-of-the-art chromatin mapping technologies.
- SnapFISH, Single-Nucleus Analysis Pipeline for multiplexed DNA FISH, to process the multiplexed DNA FISH imaging data from diverse imaging technologies and identify chromatin loops with high sensitivity, accuracy, resolution, and reproducibility.
- SnapHiC, Single-Nucleus Analysis Pipeline, to process single-cell high-throughput chromatin conformation capture (Hi-C) data and identify chromatin loops at high resolution, accuracy, sensitivity, and reproducibility from a small number of cells. Application of SnapHiC reveals cell-type-specific chromatin loops and facilitates the study of cell type-specific chromatin spatial organization in complex tissues.
- SnapHiC-D, Single-Nucleus Analysis Pipeline, for comparative analysis of single-cell high-throughput chromatin conformation capture datasets to identify differential chromatin contacts (DCCs) between cell types with high resolution, accuracy, and sensitivity. Application of SnapHiC-D demonstrates that DCCs detected in different cell types are generally associated with cell-type-specific gene expression patterns and epigenomic features.

These tools are critical in advancing understanding of the relationship between genome structure, gene regulation and disease to enable curative drug discovery and personalized medicine.