BST281: Genomic Data Manipulation, Spring 2019

Wednesday 12: Epigenetics

Epigenetic regulation: phenotypic changes induced by non-genetic modifications.

 Sometimes preserved through cell cycle and/or heritable.

 Critical in cell type differentiation.

Generally refers to nucleosome placement, histone modification, or DNA methylation.

 These influence chromatin structure, transcriptional accessibility, and promoter/enhancer activity.

Nucleosome placement is controlled to a first approximation by sequence biochemistry.

 Assayable by DNAse hypersensitivity followed by sequencing (or tiling array).

Histone modified (methylated, acetylated, phosphorylated, etc.) at multiple subunits / side chains.

 Correspond generally to activation, repression, or other conformational changes.

 Assayable by ChIP against specific modifications, typically many in the same cell population.

Generally organized into activity regions, which are themselves organized into large domains.

DNA methylation occurs at CpG dinucleotides, generally transcriptionally repressive.

 Also responsible for silencing in cell differentiation, can be aberrant in cancer.

Assayed by, among others, bisulfite sequencing.

 Convert non-methylated Cs to Us, sequence differences.

 Analyzed as % methylation followed by smoothing, peak finding, and differential methylation analysis.

Chromatin capture assays identify long-distance contacts between DNA segments.

 Hi-C sequences region pairs after cross-linking, ChIA-PET pulls down only those bound by cofactor.

# Textbooks

Chromatin organization: Pevsner, Chapter 16 p639-683

# Literature

[Comprehensive mapping of long-range interactions reveals folding principles of the human genome. Lieberman-Aiden, Science 2009](https://www.ncbi.nlm.nih.gov/pubmed/19815776)

[Determinants and dynamics of genome accessibility. Bell, NRG 2011](https://www.ncbi.nlm.nih.gov/pubmed/21747402)

[Mapping and analysis of chromatin state dynamics in nine human cell types. Ernst, Nature 2011](https://www.ncbi.nlm.nih.gov/pubmed/21441907)

[Methodological aspects of whole-genome bisulfite sequencing analysis. Adusumalli, BiB 2015](https://www.ncbi.nlm.nih.gov/pubmed/24867940)