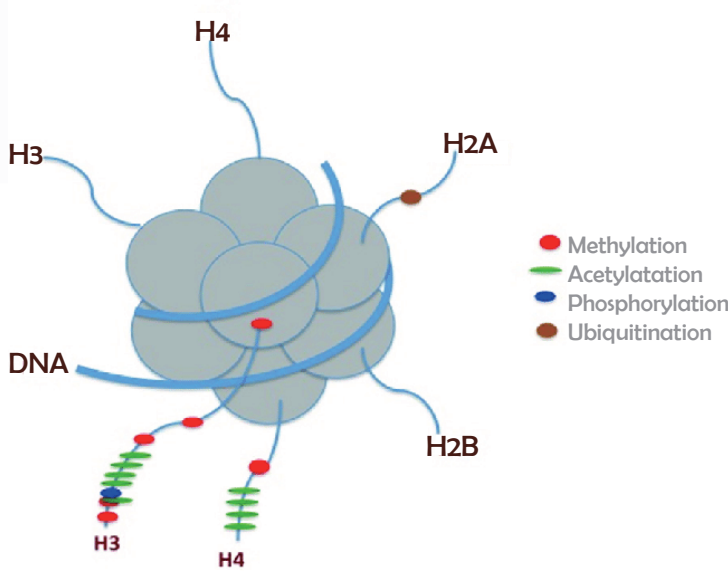
Genome-Wide Profiling of Histone Modifications with ChIP-Seq

CD Genomics
The Genomics Services Company

Introduction to Histone Modifications

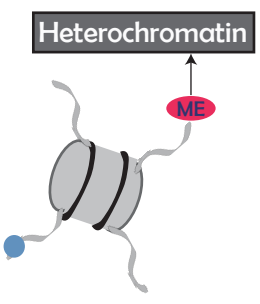
Histone can be covalently post-translational modified. At least nine different types of post-translational modifications (PTMs) to histones have been identified, such as methylation, acetylation, phosphorylation, ubiquitylation, and sumoylation. Histone modifications change chromatin structures or recruit histone modifiers, causing change in gene expressions. The PTMs are involved in diverse biological processes including transcriptional regulation, chromosome packaging, and DNA damage/repair. Thus, profiling of various histone modifications would provide important information to better understand the epigenetic mechanisms underlying cellular processes and the development of drugs targeting histone and their modifications.

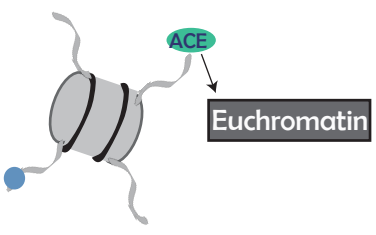


Five Major Types of Histone Modifications

Histone Methylation

Histone can be methylated on lysine residues, which can be mono-, di- or trimethylated, and arginine residues, which can be mono- or dimethylated. Histone methylation affects transcriptional activity, depending on the number of methyl groups and position of the amino acid being modified.



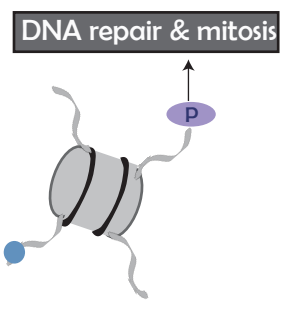


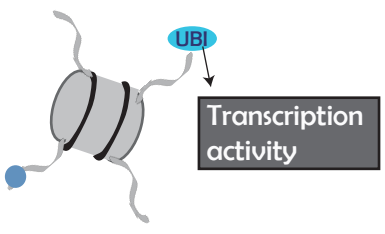
Histone Acetylation

Lysine can be acetylated on the N-terminal tails of core histones. Lysine acetylation reduces the affinity between a histone protein and DNA, hence increasing gene expression. It also recruits nucleosome-remodeling complexes to promote and maintain enchromatin structure.

Histone Phosphorylation

Histone phosphorylation occurs at serine, threonine and tyrosine residues. Many serine and threonine phosphorylation events are involved in DNA repair or mitosis, but some play a part in epigenetic regulation of transcription.



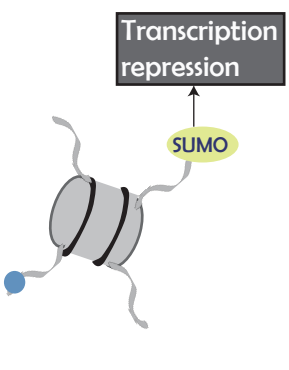


Histone Ubiquitylation

Histone ubiquitylation is a modification with ubiquitin moiety comprising of a 76-amino-acid peptide. It can affect transcription activity, nucleosome stability and gene accessibility.

Histone Sumoylation

Histone Sumoylation can stabilize proteins, change subcellular localization, impact enzyme activity and regulate interactions with other proteins. Many transcription factors and cofactors can be sumoylated, which generally indicates transcription repression.



ChIP-Seq: A Versatile Tool For Histone Modification Studies

WHAT IS CHIP-SEQ?

ChIP-seq is one of the most important techniques for genome-wide profiling of DNA-binding proteins, histone modifications or nucleosomes. It offers higher resolution, less noise, and greater coverage compared to ChIP-chip.

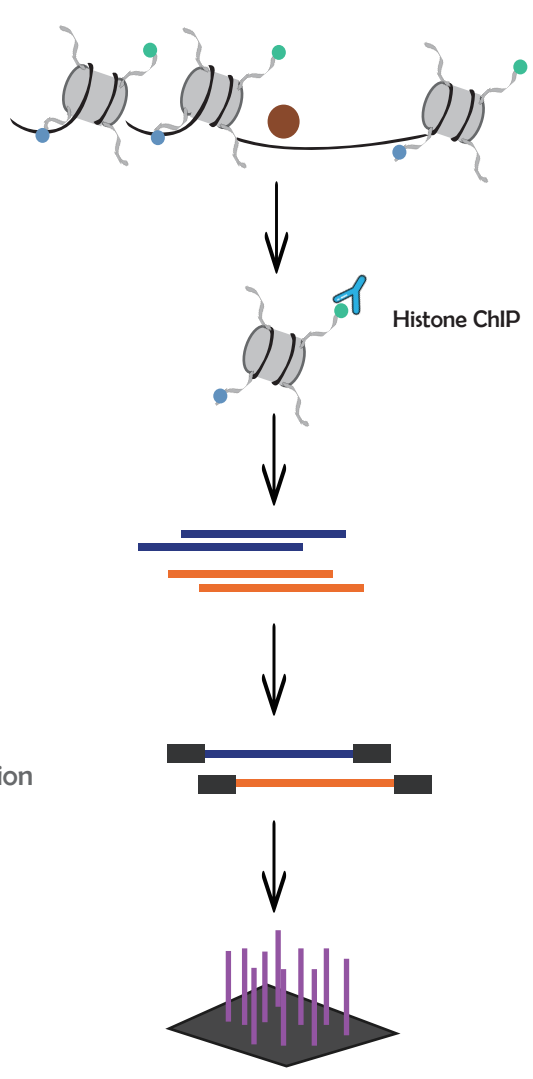
HOW DOES CHIP-SEQ WORK?

In a ChIP experiment, the DNA-binding protein iscrosslinked to DNA, and the chromatin is sheared into 200-600 bp fragments. An antibody specific to the protein of interest is used for immunoprecipitation.

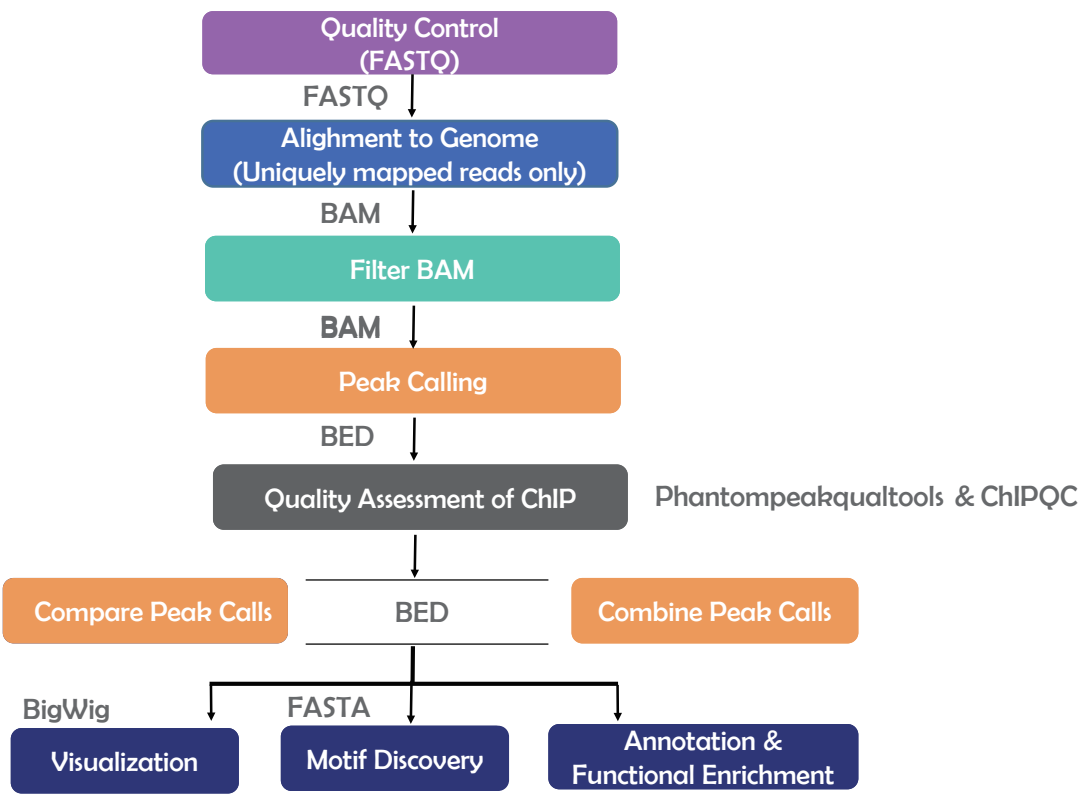
DNA release:
The crosslinks are reversed and the DNA is released.

Librabry preparation:
End repair, adapter ligation, library amplification

NGS and data analysis:
SE50 or PE150, quality control insights, read mapping, methylation calling and differential methylation analysis.



CHIP-SEQ DATA ANALYSIS



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