# Prediction of Regulatory Networks from Expression and Chromatin Data

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Deutsches Forschungszentrum für Gesundheit und Umwelt

## **Overview**

Time	Topic	Who
2:30 - 2:45	Introduction / gene regulation / transcription / chromatin	IC
2:45 - 3:00	Introduction ChIP-seq peak calling	MH
3:00 - 3:50	Practical peak calling	MH
4:15 - 4:30	Introduction Footprints	IC
4:30 - 4:45	Introduction Regulatory networks	MS
4:45 - 5:50	Practical Regulatory Networks	IG, MS & FS
5:50 - 6:00	Q & A session	all

#### Material - https://github.com/SchulzLab/EpigenomicsTutorial-ISMB2017

#### **Team**



Ivan Costa (IC)



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# Introduction - Gene Regulation, Transcription and Chromatin

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www.costalab.org

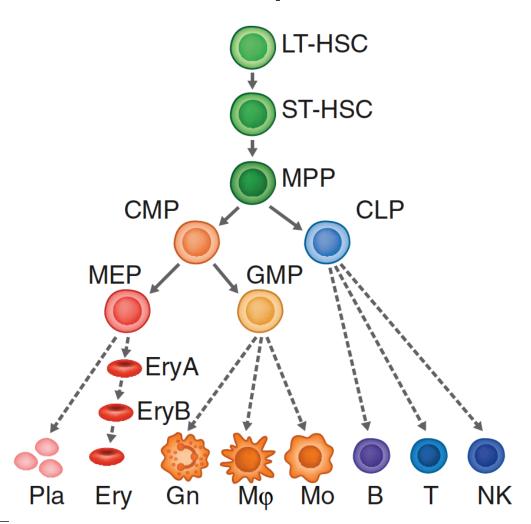






## Cell Differentiation & Gene Regulation

#### **Hematopoiesis**

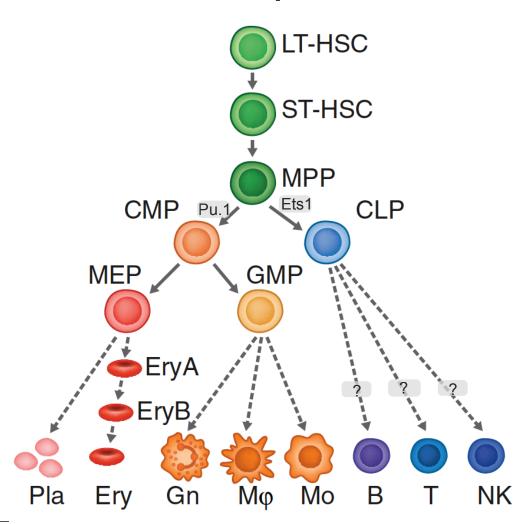


plasticity cell memory



# **Cell Differentiation & Gene Regulation**

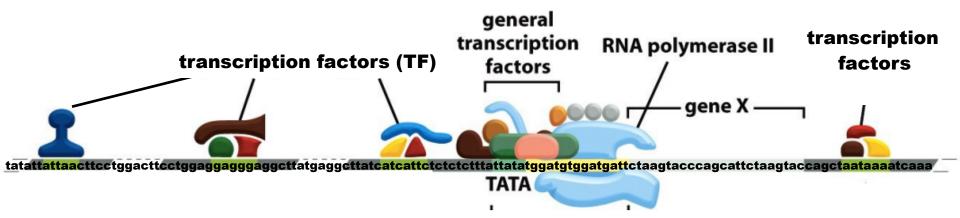
#### **Hematopoiesis**



plasticity cell memory

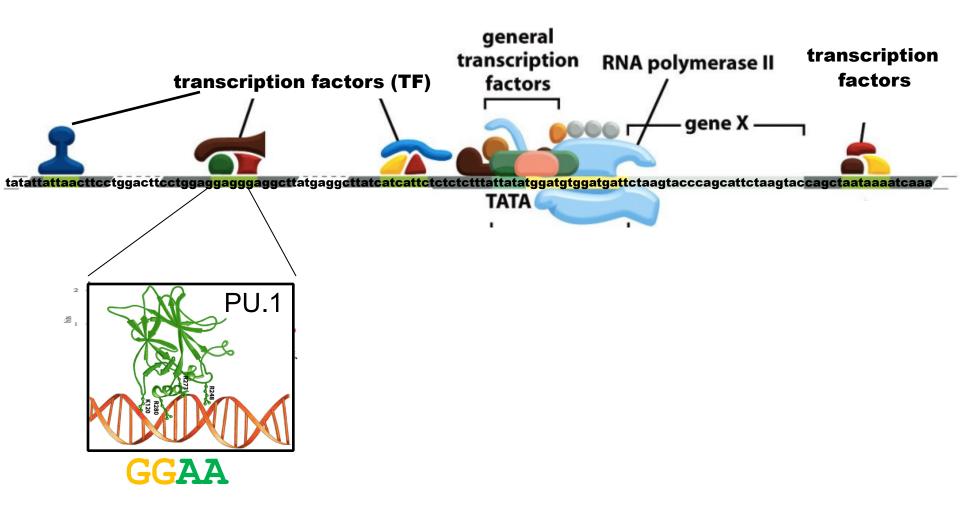


# Regulatory Control – Protein-DNA interaction



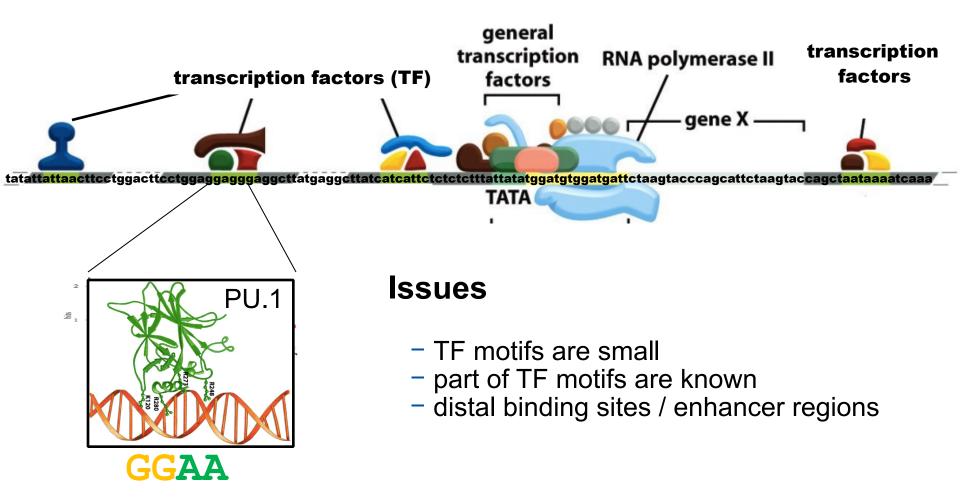


# Regulatory Control – Protein-DNA interaction



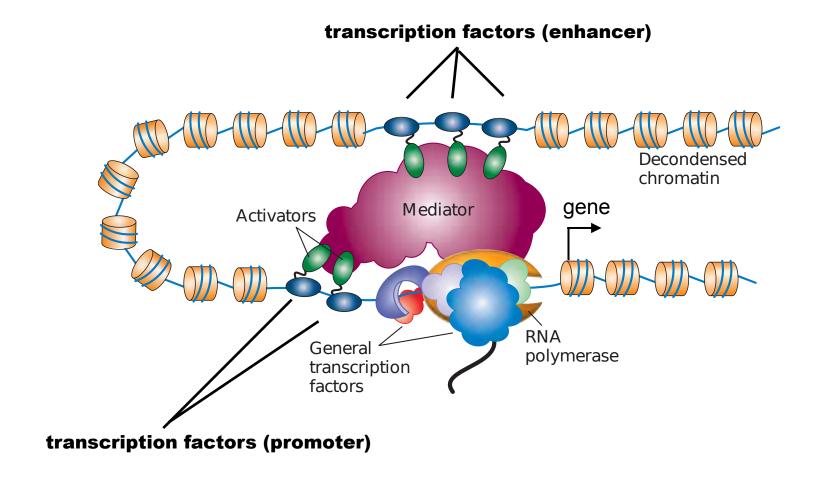


# Regulatory Control – Protein-DNA interaction





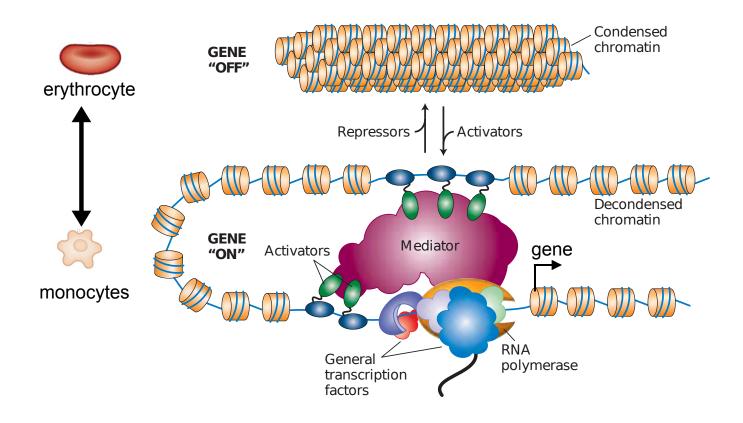
## **Chromatin and Gene Regulation**





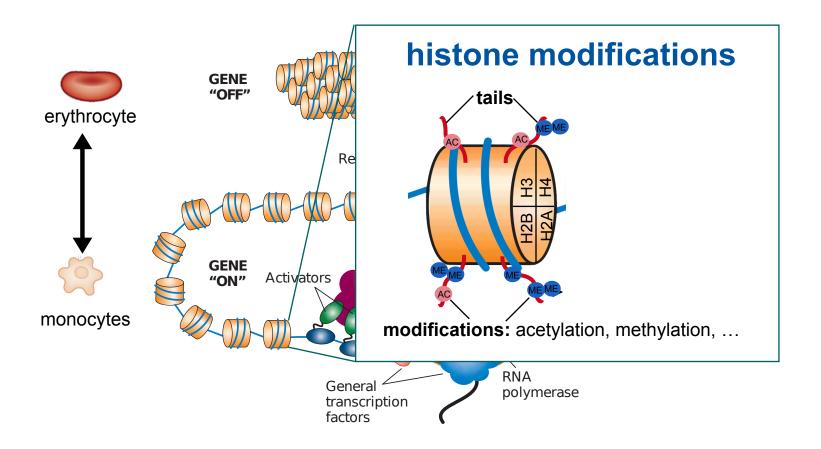


# **Chromatin and Cell Memory/Plasticity**



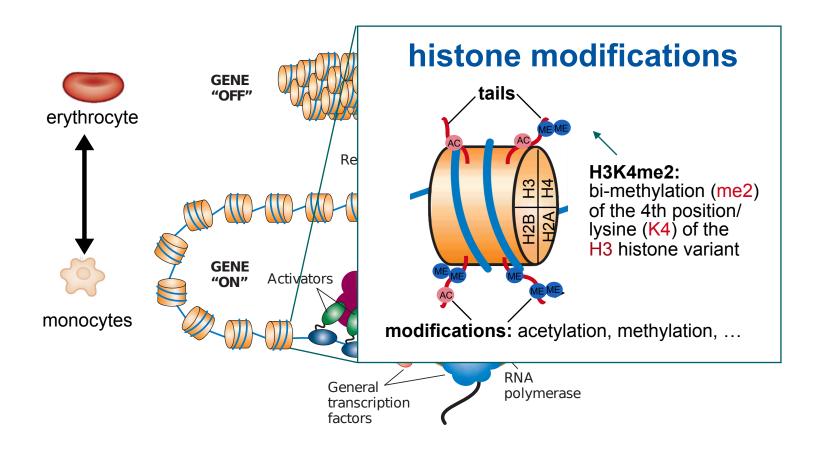


## **Chromatin and Histones**



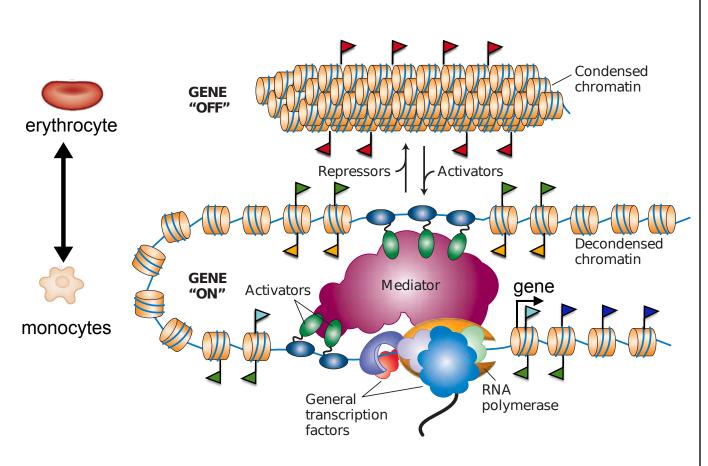


#### **Chromatin and Histones**





# **Chromatin and Cell Memory/Plasticity**



#### Histone Code

**Transcription** 

H3K79me2, H3k36me3

Active Regions

H3K27ac, H3K9ac

Active Promoters

H3K4me3

Active Enhancers

H3K4me1

Repressed Prom.

H3K27me3

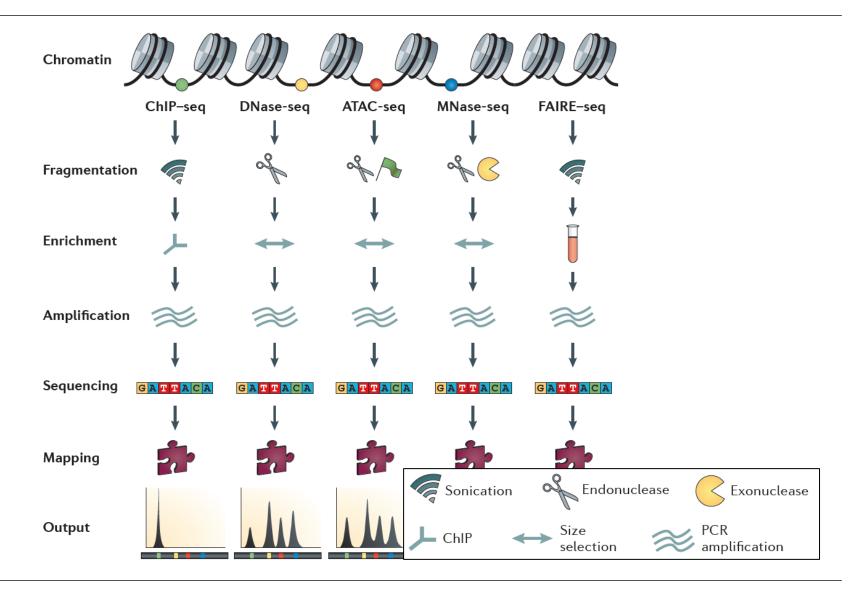
Repressed Regions

H3K9me3





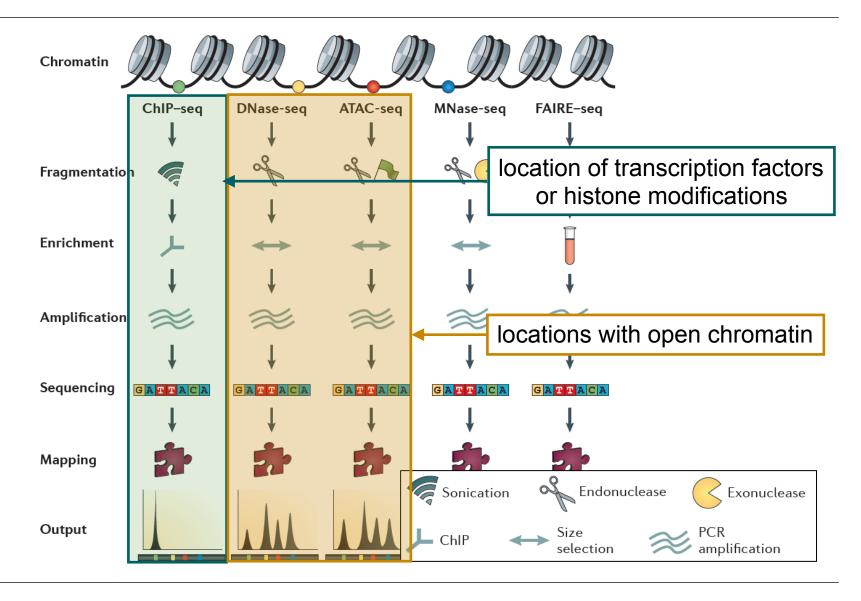
#### **NGS** and Chromatin





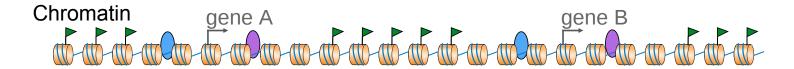


#### **NGS** and Chromatin



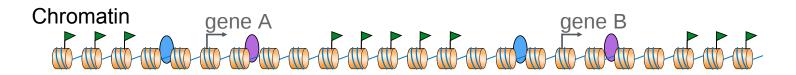


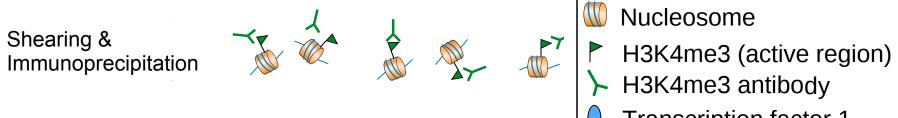




- Nucleosome
- ► H3K4me3 (active region)
- ► H3K4me3 antibody
- Transcription factor 1
- Transcription factor 2



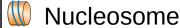






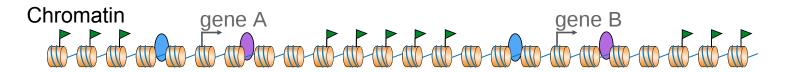




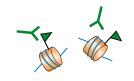


- Transcription factor 1
- Transcription factor 2





Shearing & Immunoprecipitation

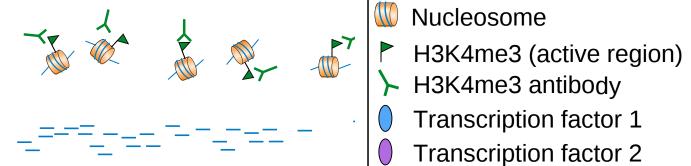








Sequencing

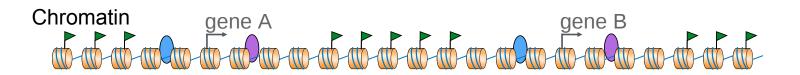




Nucleosome

- - Transcription factor 2

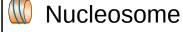


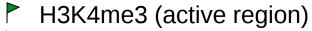


Shearing & Immunoprecipitation









► H3K4me3 antibody



Transcription factor 2

Sequencing



Alignment



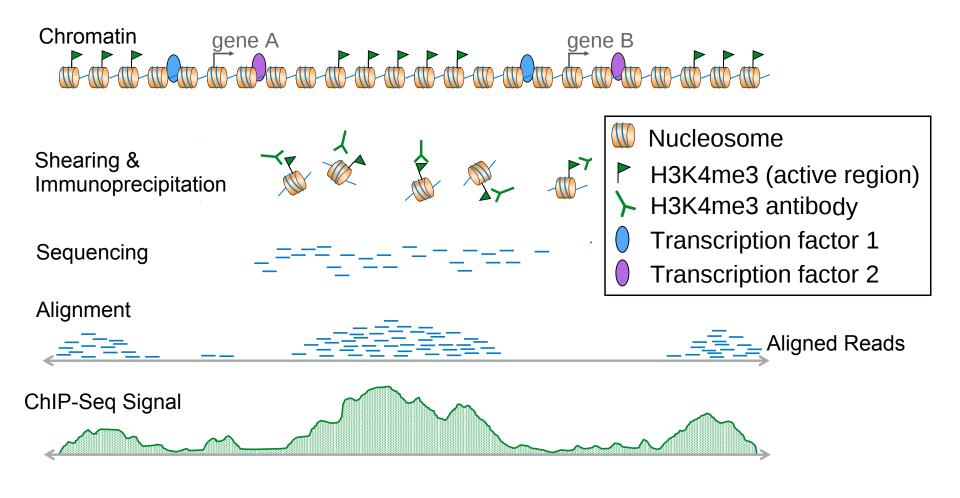




Aligned Reads

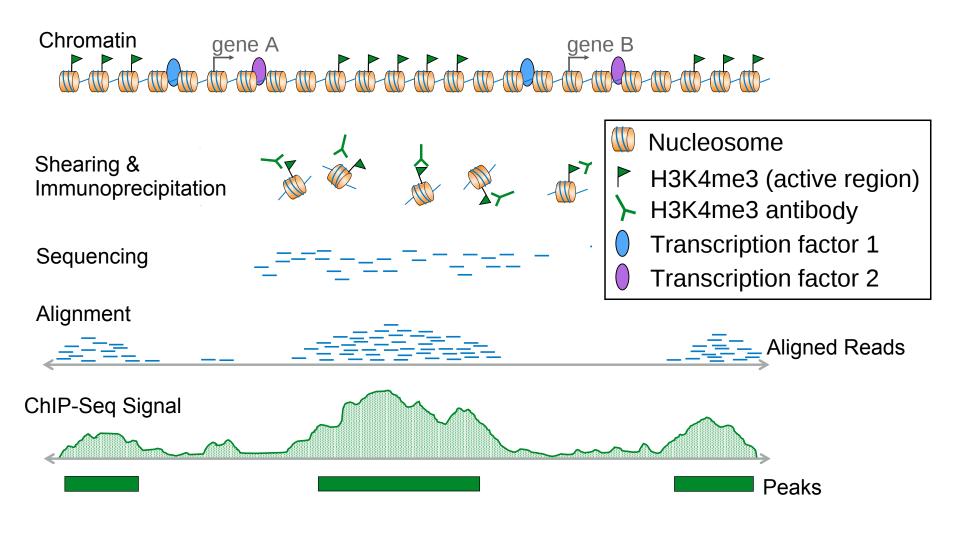






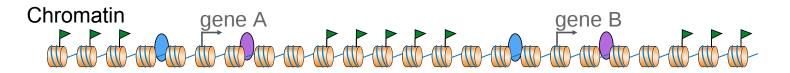




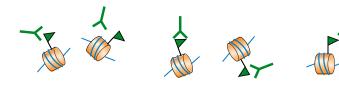








Shearing & immunoprecipitation



Sequencing





**Nucleosome** 

- H3K4me3 (active region)
- ► H3K4me3 antibody
- Transcription factor 1
  - Transcription factor 2

Alignment



## ChIP-Seq

ChIP-Seq S



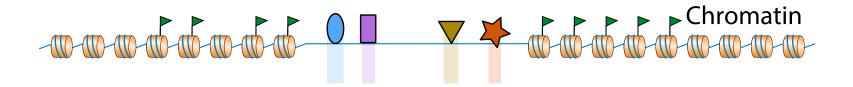
- detect location of TF and histone modifications with moderate precision (+/- 50-100 bps)

- one experiment per protein of interest
- not possible for all proteins

Reads







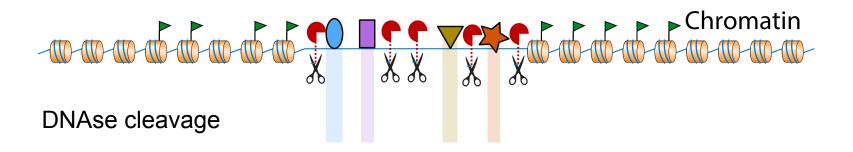
Nucleosome

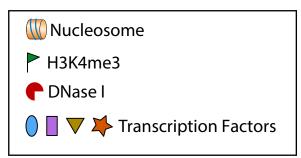
H3K4me3

P DNase I



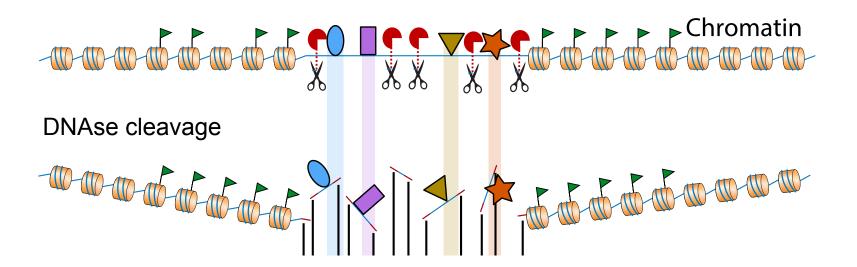


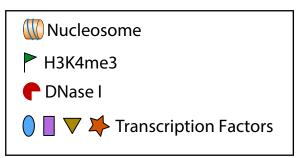






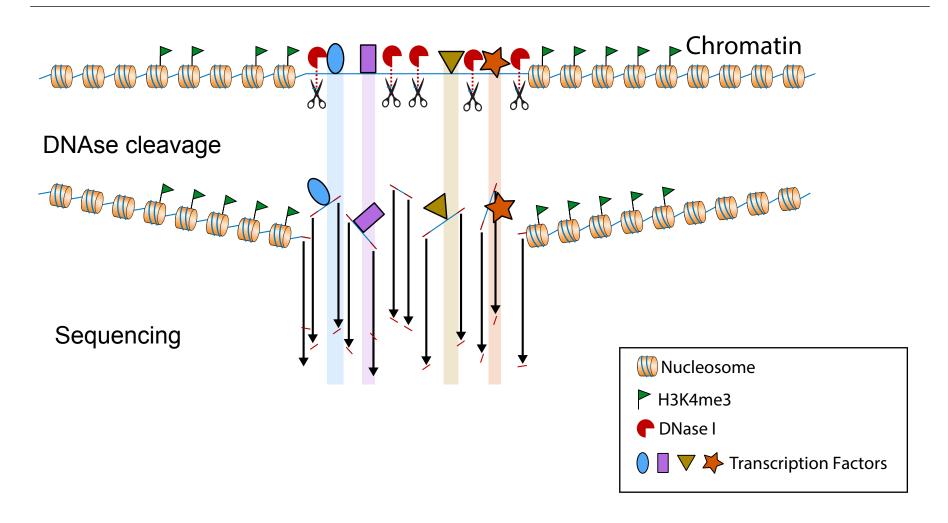




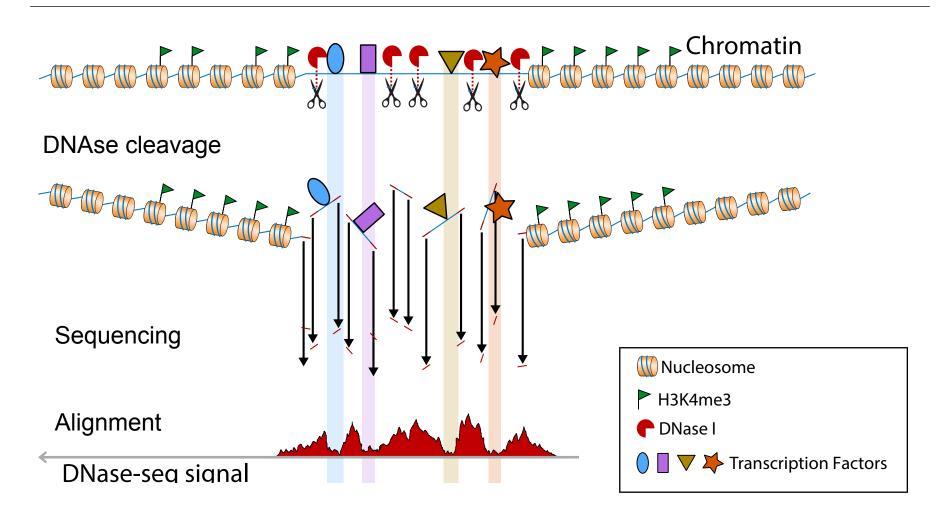




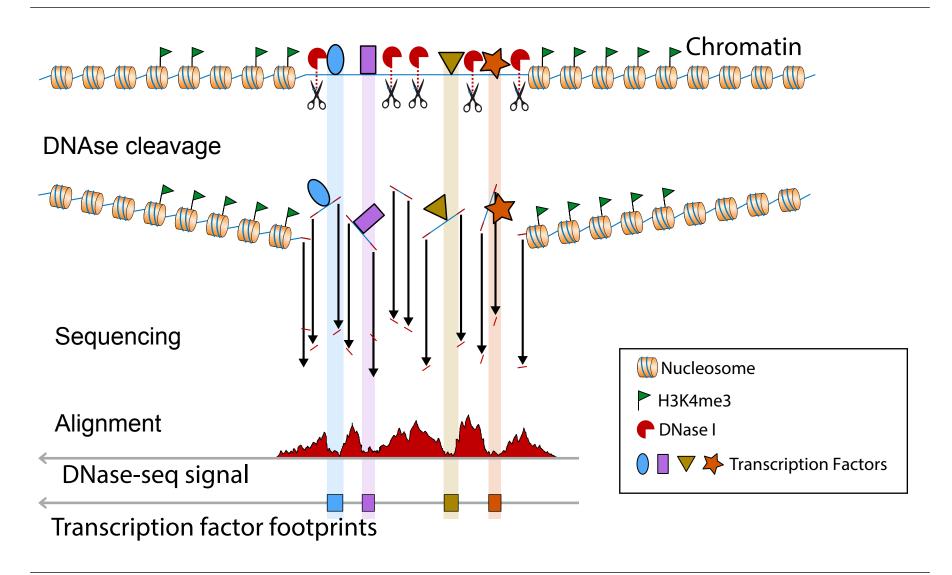






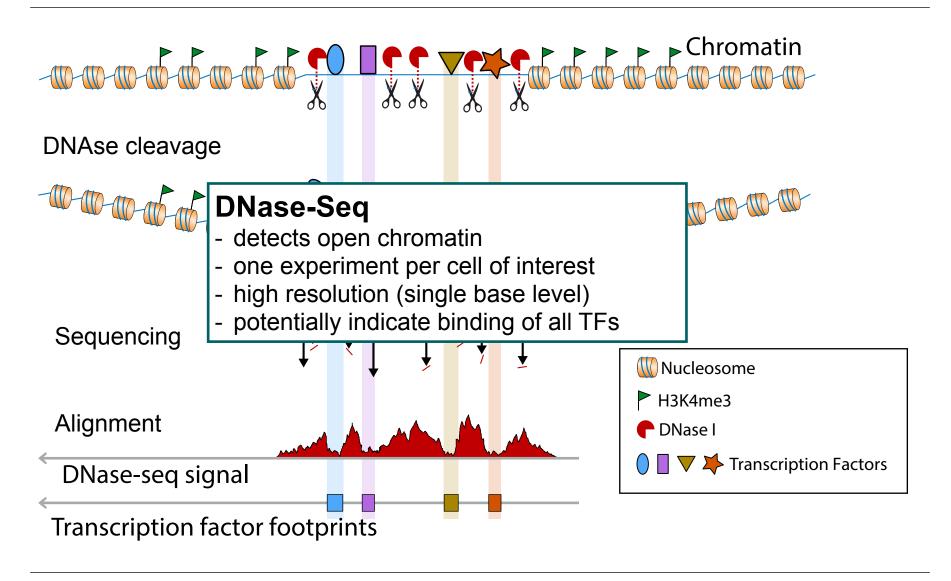
















#### **Overview**

#### **Transcription factors**

- main player of gene regulation/transcription

#### **Chromatin/histones**

 organization of chromatin conformation and controls cellular memory/plasticity

#### **Histone modifications**

- affect interaction of histones with DNA and other histones
- indicate regulatory status of genomic regions

## **Next generation sequencing**

- TF binding and histone modifications (ChIP-seq)
- open chromatin regions (DNase- & ATAC-seq)





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