

Prediction of Regulatory Networks from Expression and Chromatin Data

Ivan G. Costa, RWTH Aachen University, Germany

Marcel Schulz, Saarland University & Max Planck Institute for Informatics,
Germany

Matthias Heinig, Helmholtz Center Munich, Germany



Overview

Goals

- use chromatin information to define cell specific regulatory regions
- inference of regular networks driving development and disease progression

Learning Objectives

- use differential peak calling (*histoneHMM*) to find changes in chromatin (ChIP-seq) and define regulatory regions
- use computational footprinting (*HINT*) on open chromatin (ATAC-seq) to find cell specific transcription factor (TF) binding sites
- regulatory network inference (*TEPIC*) with integrative analysis of expression, chromatin and TF binding

Schedule

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 & JH
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)



Matthias Heinig (MH)



Johann Hawe



Marcel Schulz(MH)



Florian Schmidt (FS)

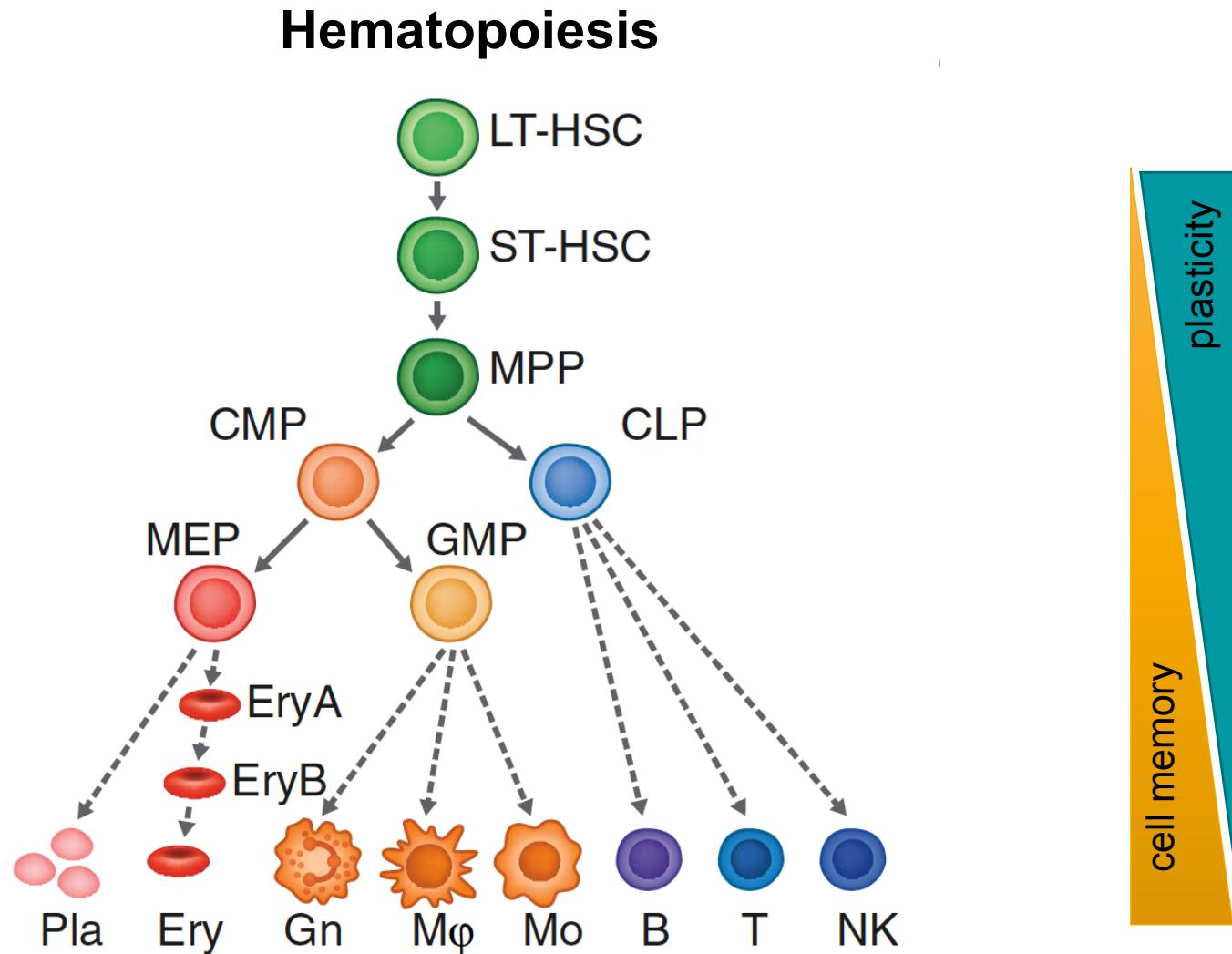
Introduction - Gene Regulation, Transcription and Chromatin

Ivan G. Costa
RWTH Aachen University, Germany

www.costalab.org

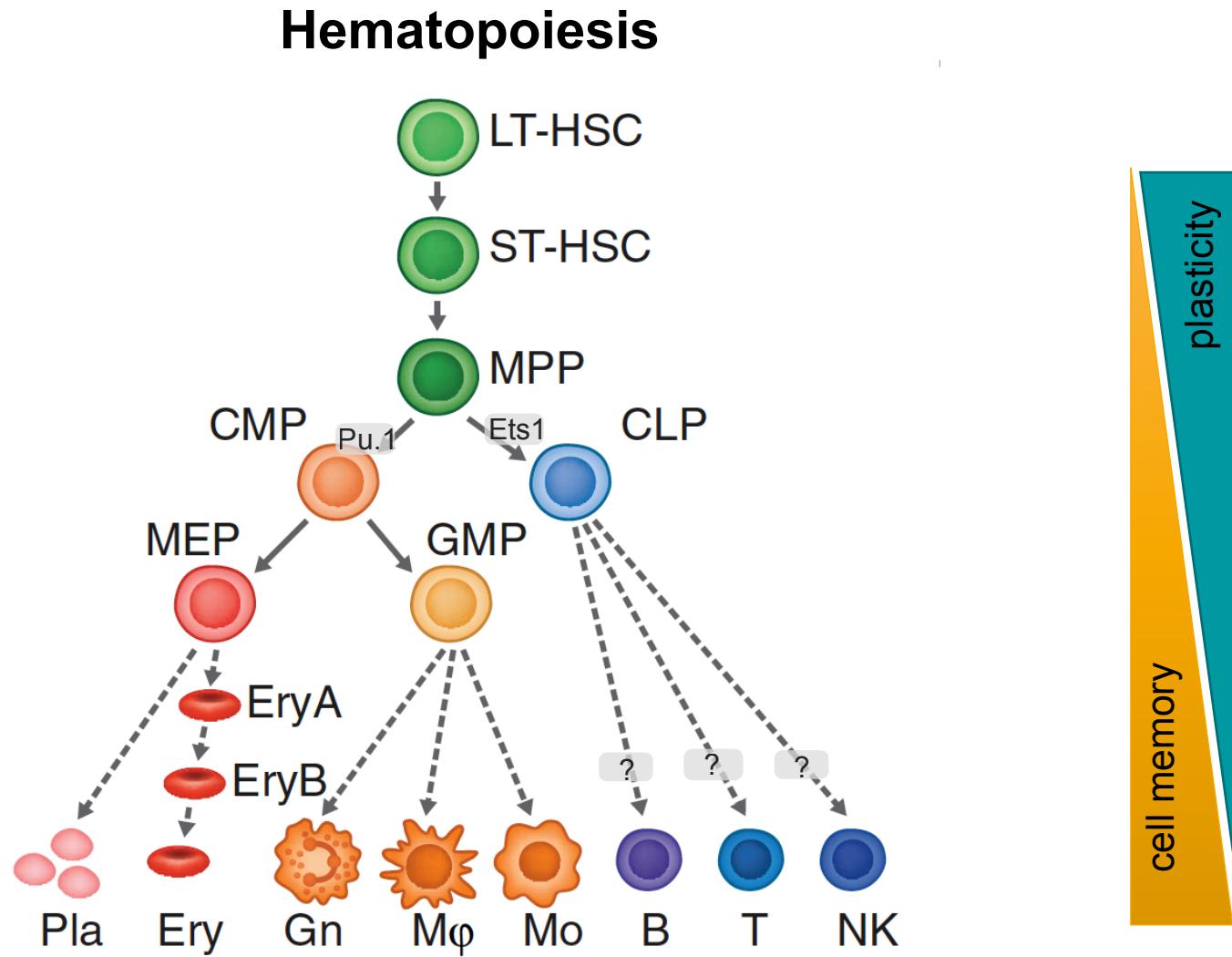


Cell Differentiation & Gene Regulation



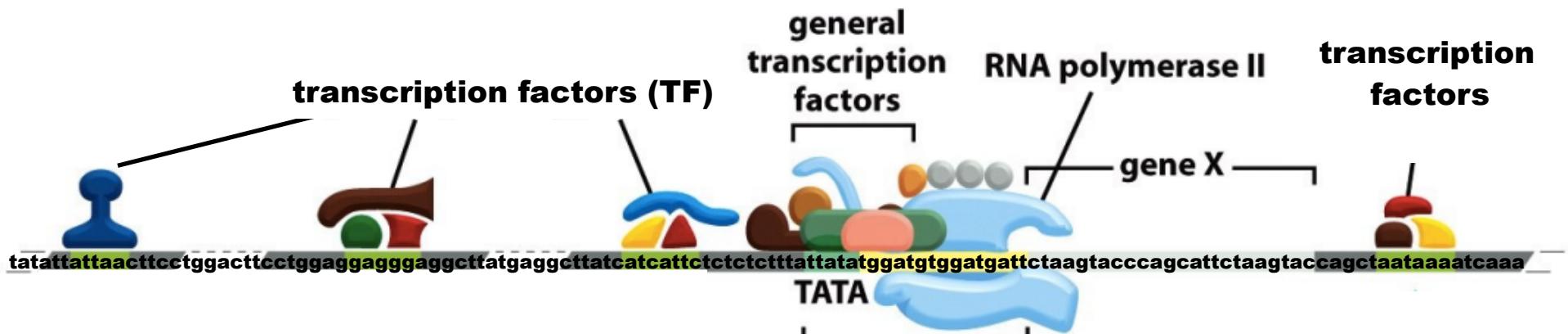
Adapted from Lara-Astiaso, Science, 2015.

Cell Differentiation & Gene Regulation

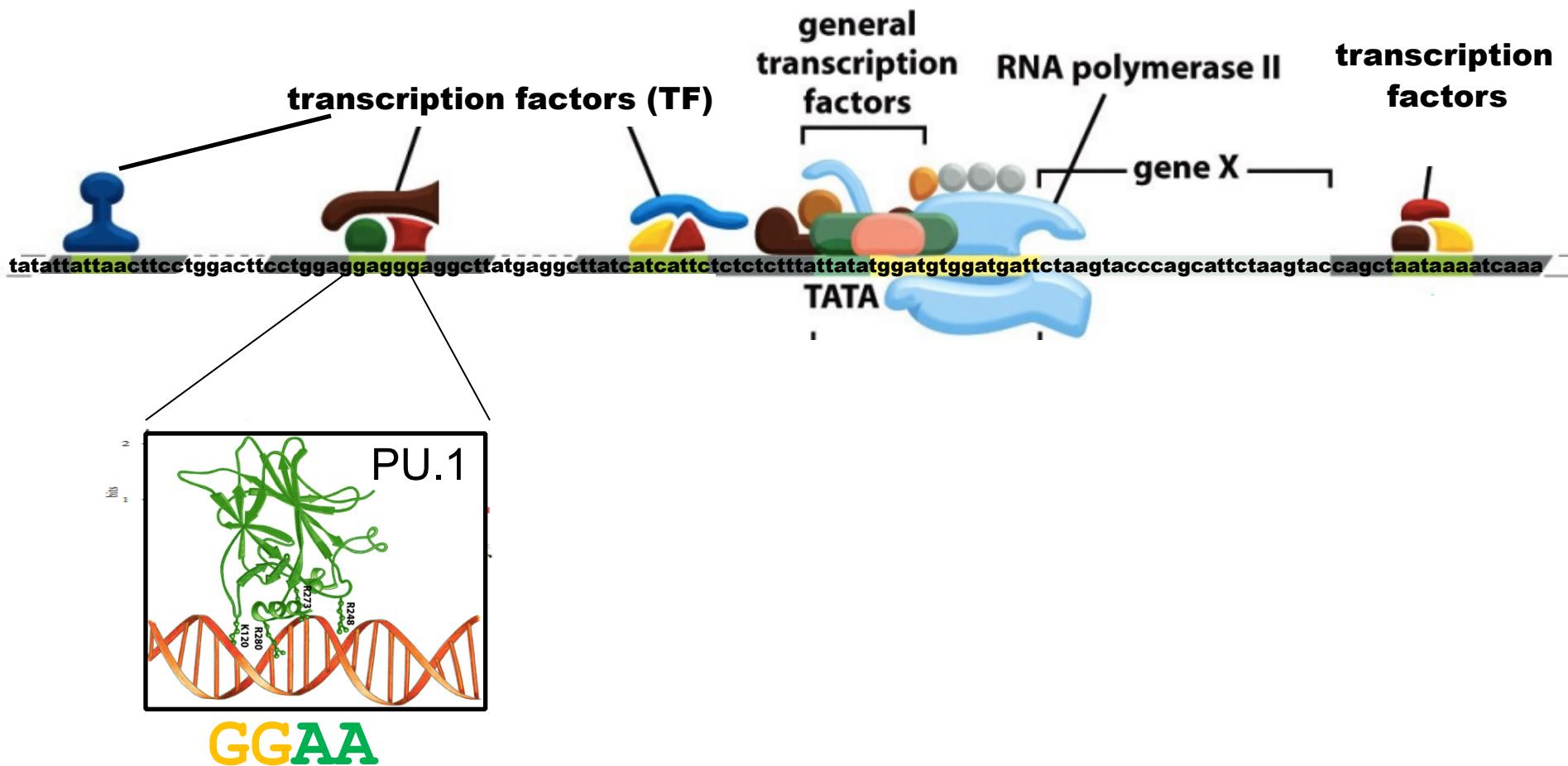


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Regulatory Control – Protein-DNA interaction

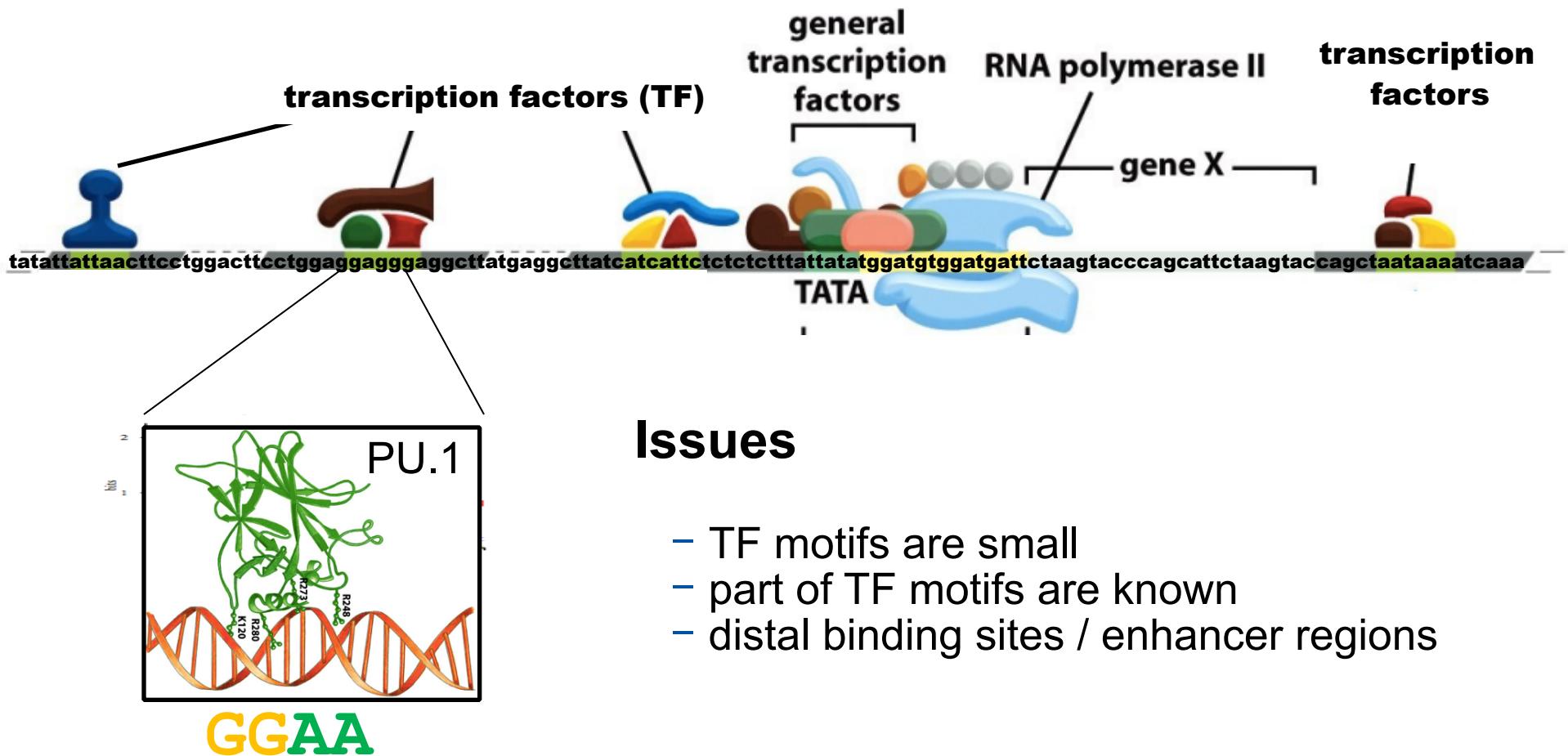


Regulatory Control – Protein-DNA interaction



Adapted from Alberts, B. et al. (2008) Garland Science, 5th ed.

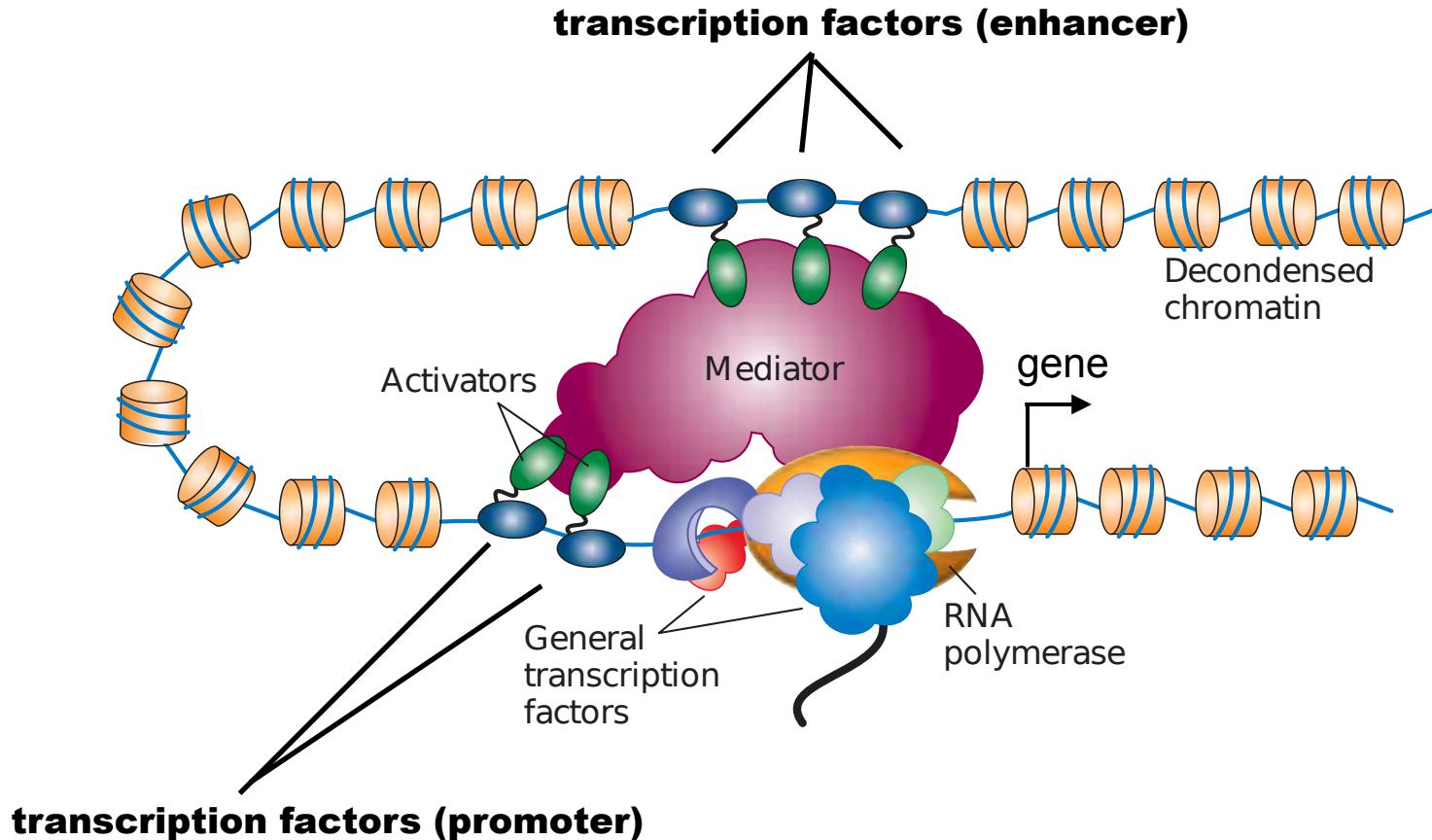
Regulatory Control – Protein-DNA interaction



Issues

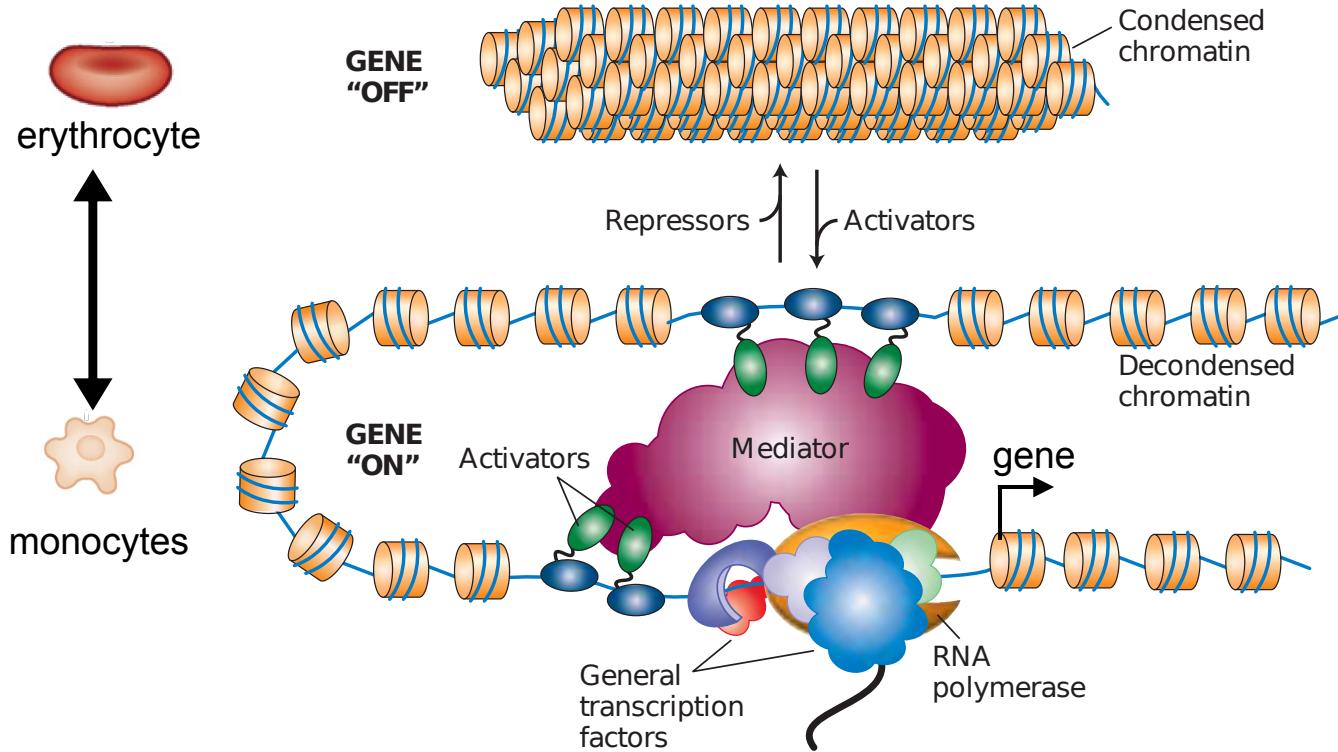
- TF motifs are small
- part of TF motifs are known
- distal binding sites / enhancer regions

Chromatin and Gene Regulation

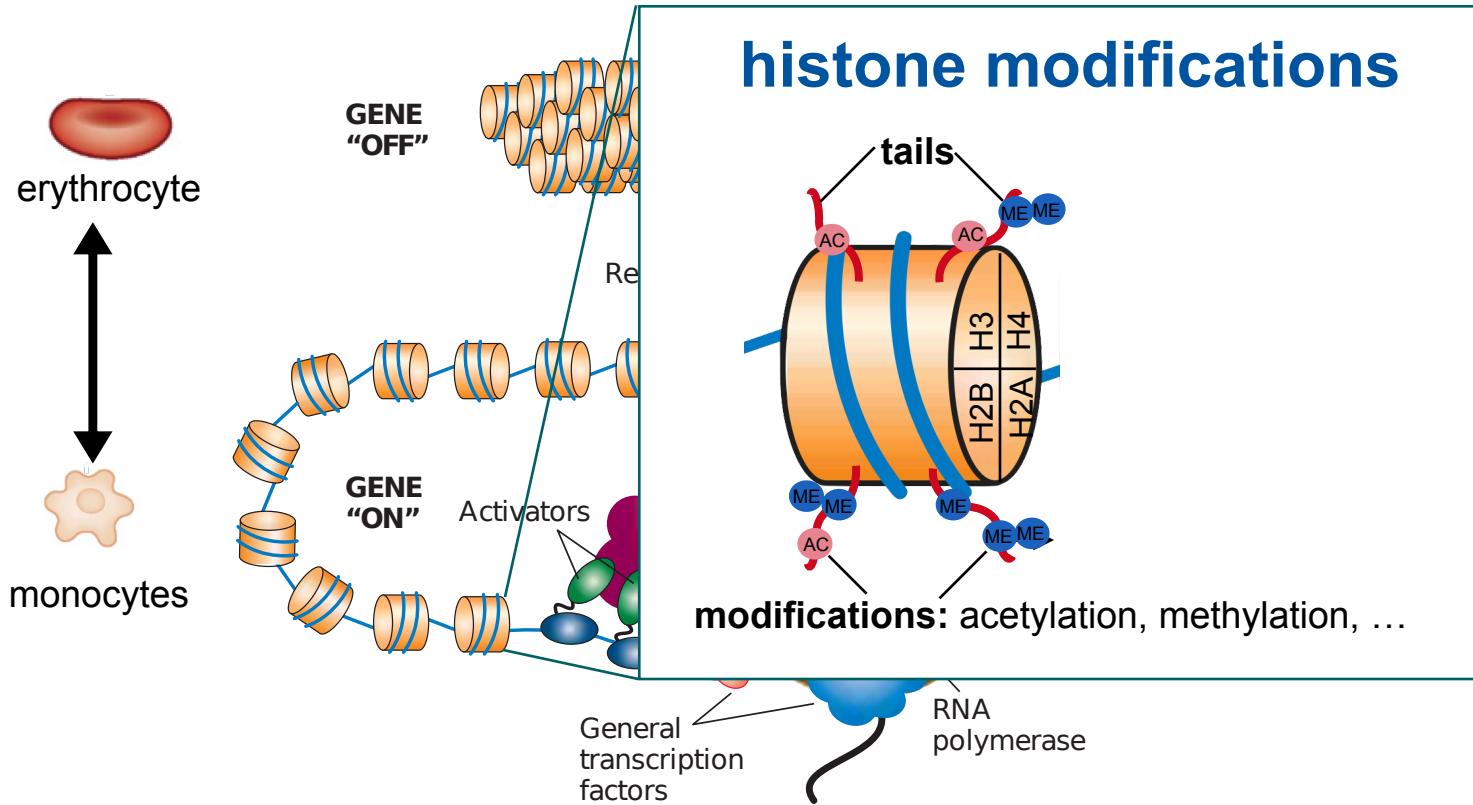


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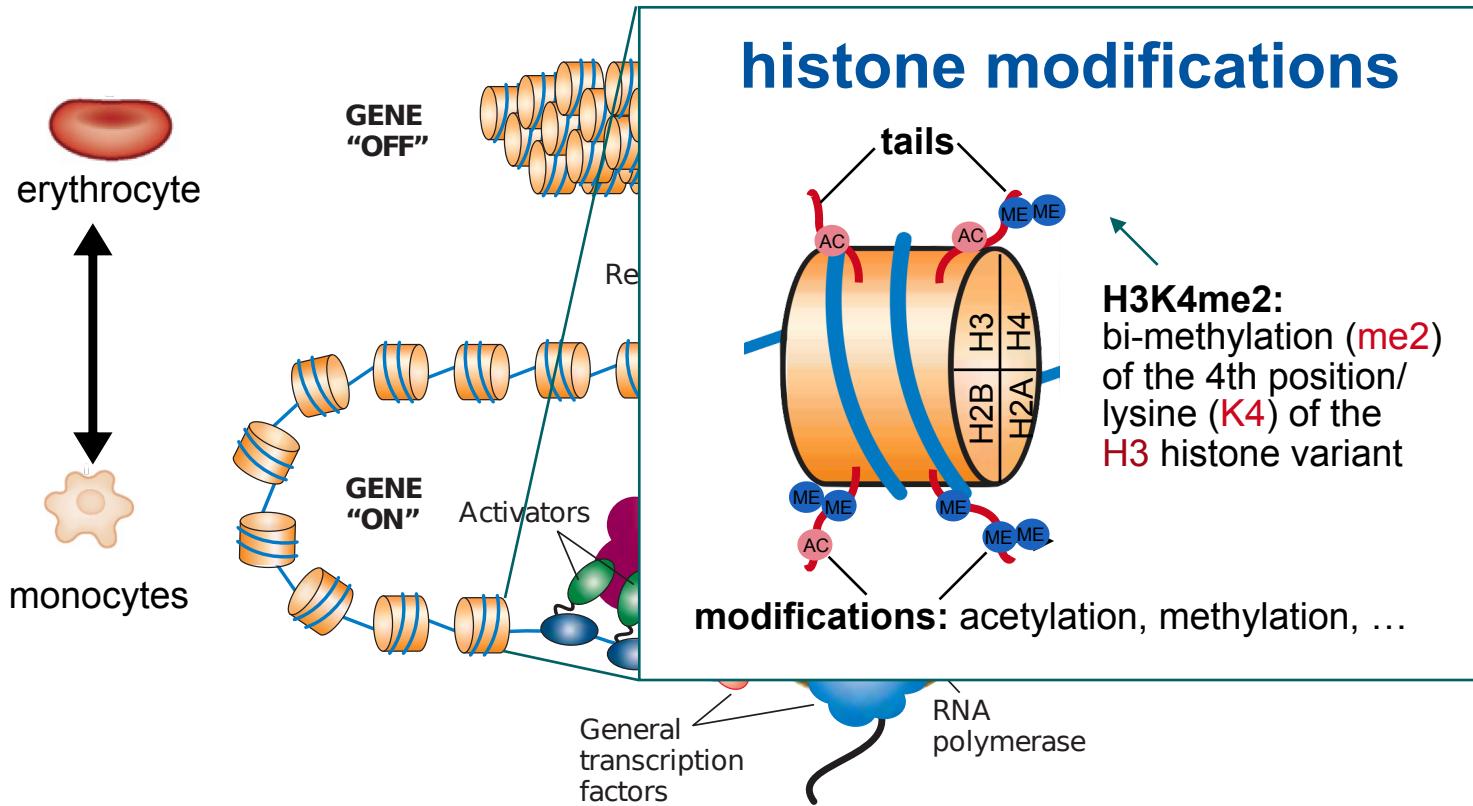
Chromatin and Cell Memory/Plasticity



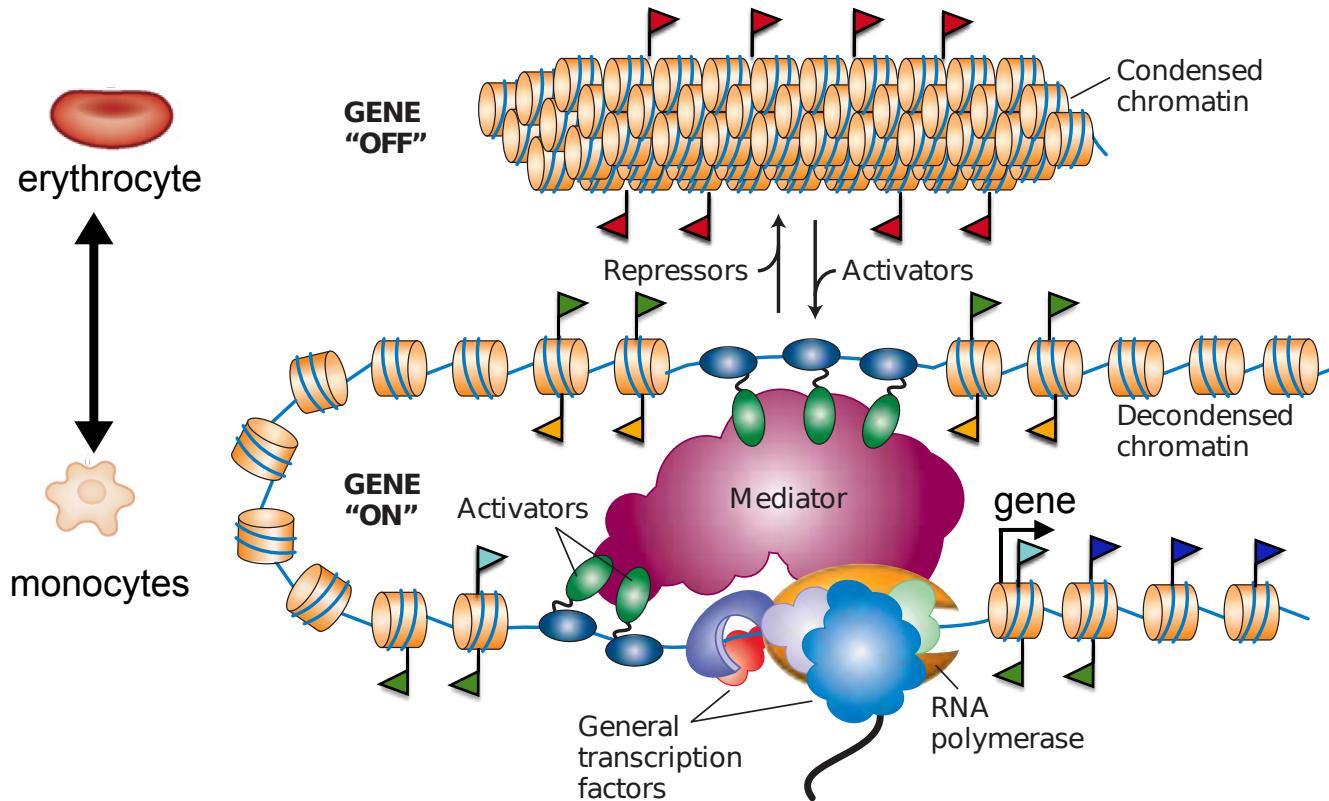
Chromatin and Histones



Chromatin and Histones



Chromatin and Cell Memory/Plasticity



Histone Code

► Transcription

H3K79me2, H3k36me3

► Active Regions

H3K27ac, H3K9ac

► Active Promoters

H3K4me3

► Active Enhancers

H3K4me1

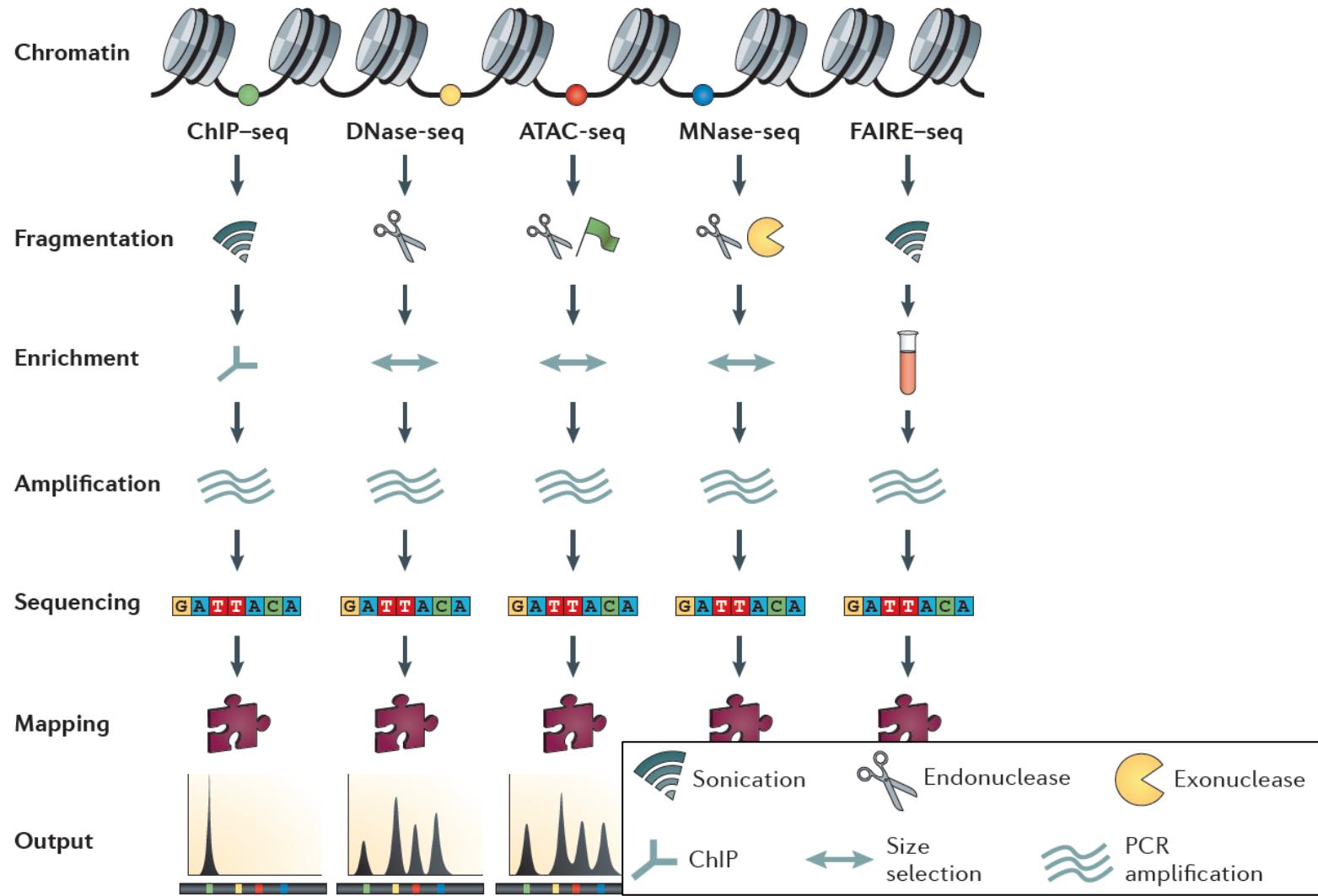
► Repressed Prom.

H3K27me3

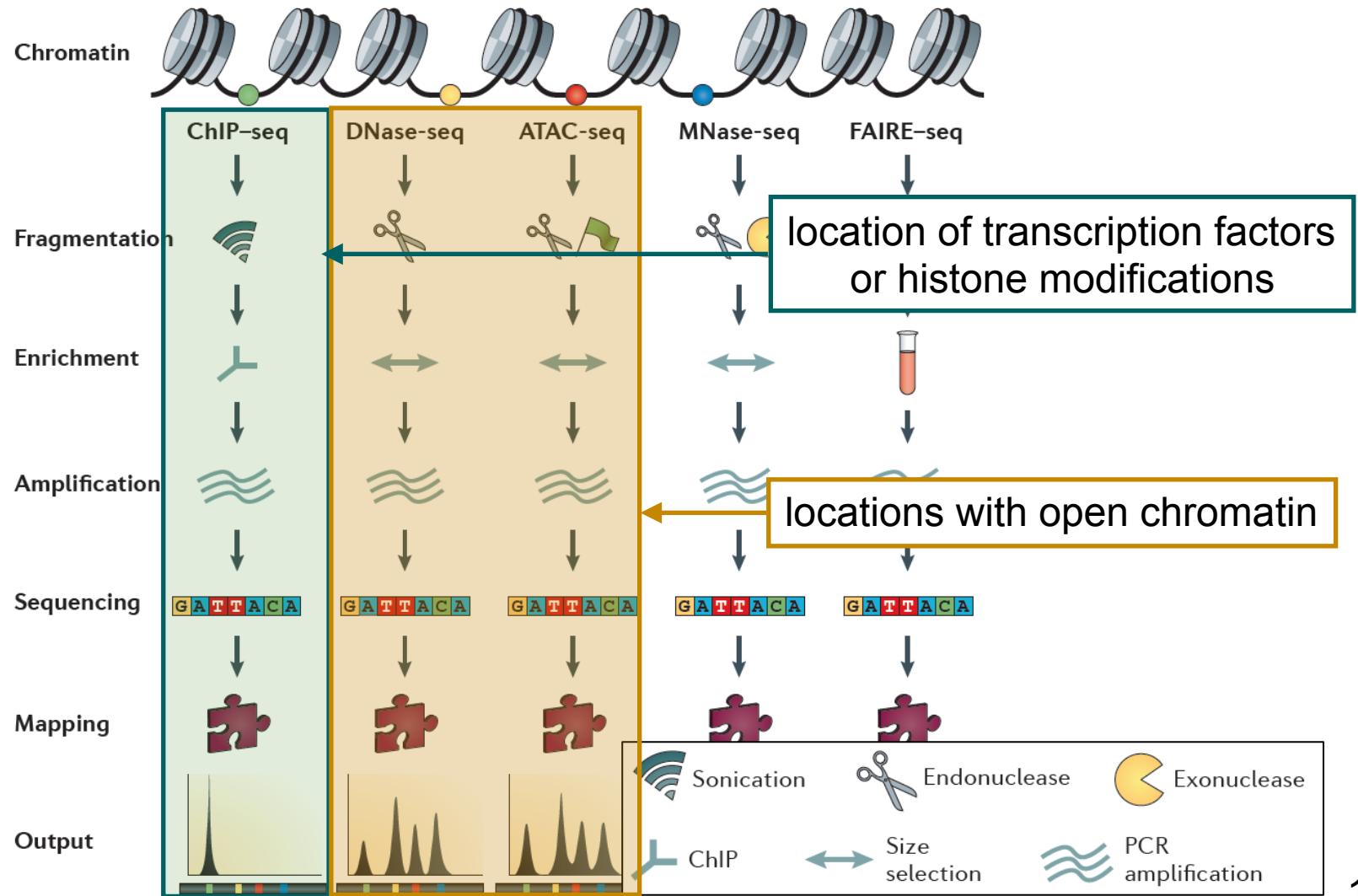
► Repressed Regions

H3K9me3

NGS and Chromatin

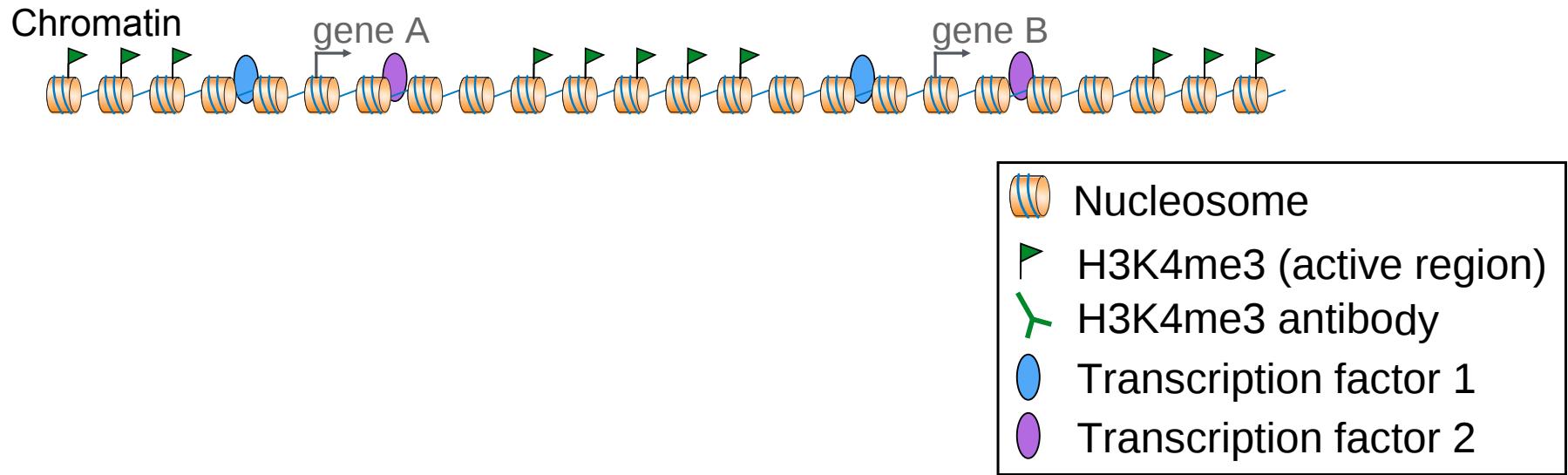


NGS and Chromatin

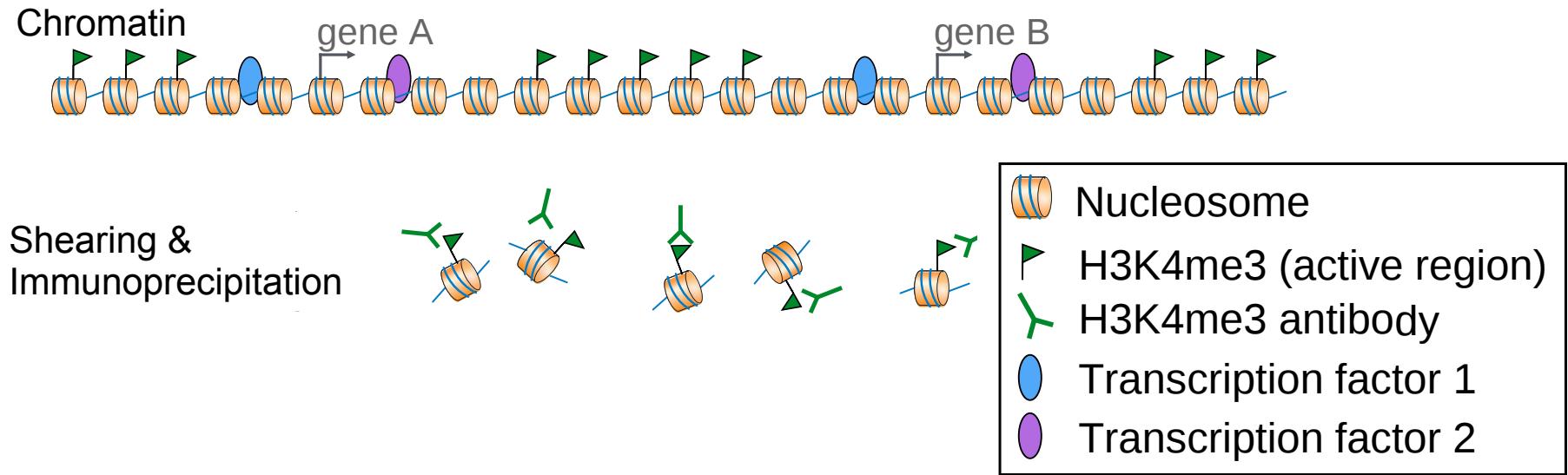


Source: Meyer, C.A. and Liu X.S. (2014). *Nature Reviews Genetics*.

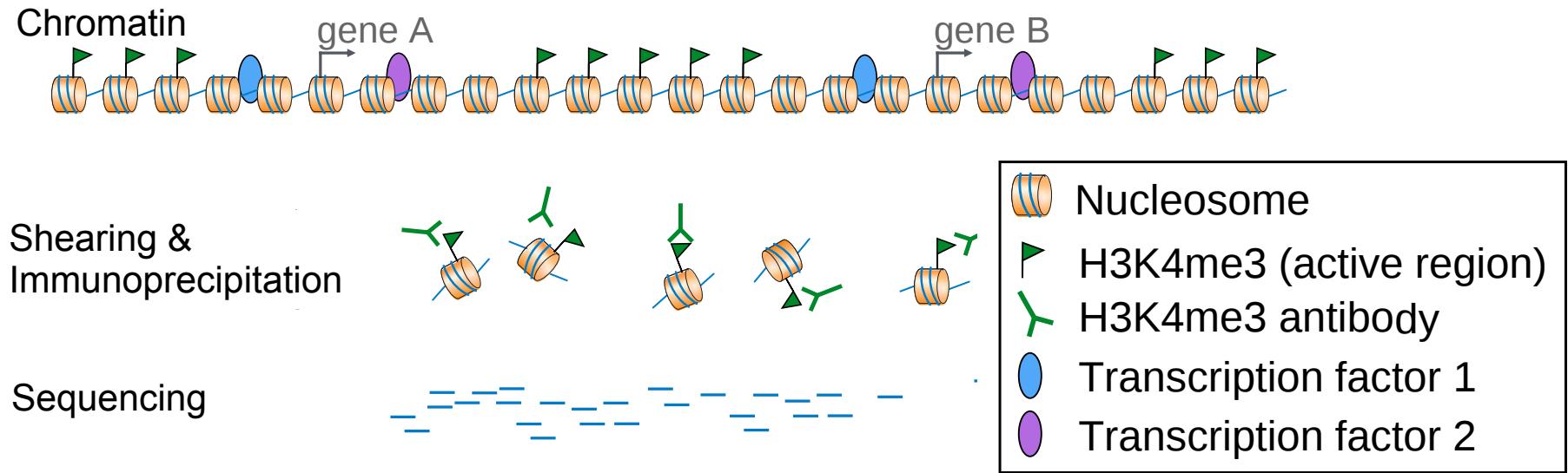
DNA - Protein interactions with ChIP-Seq



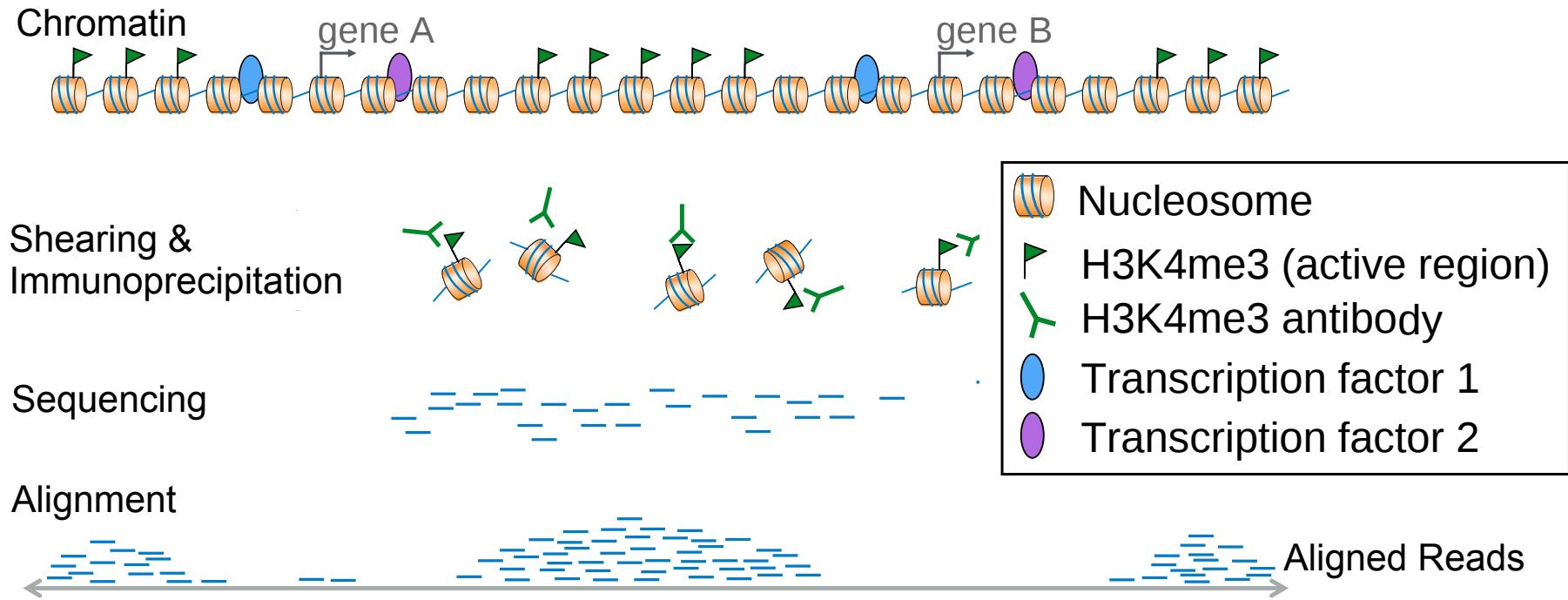
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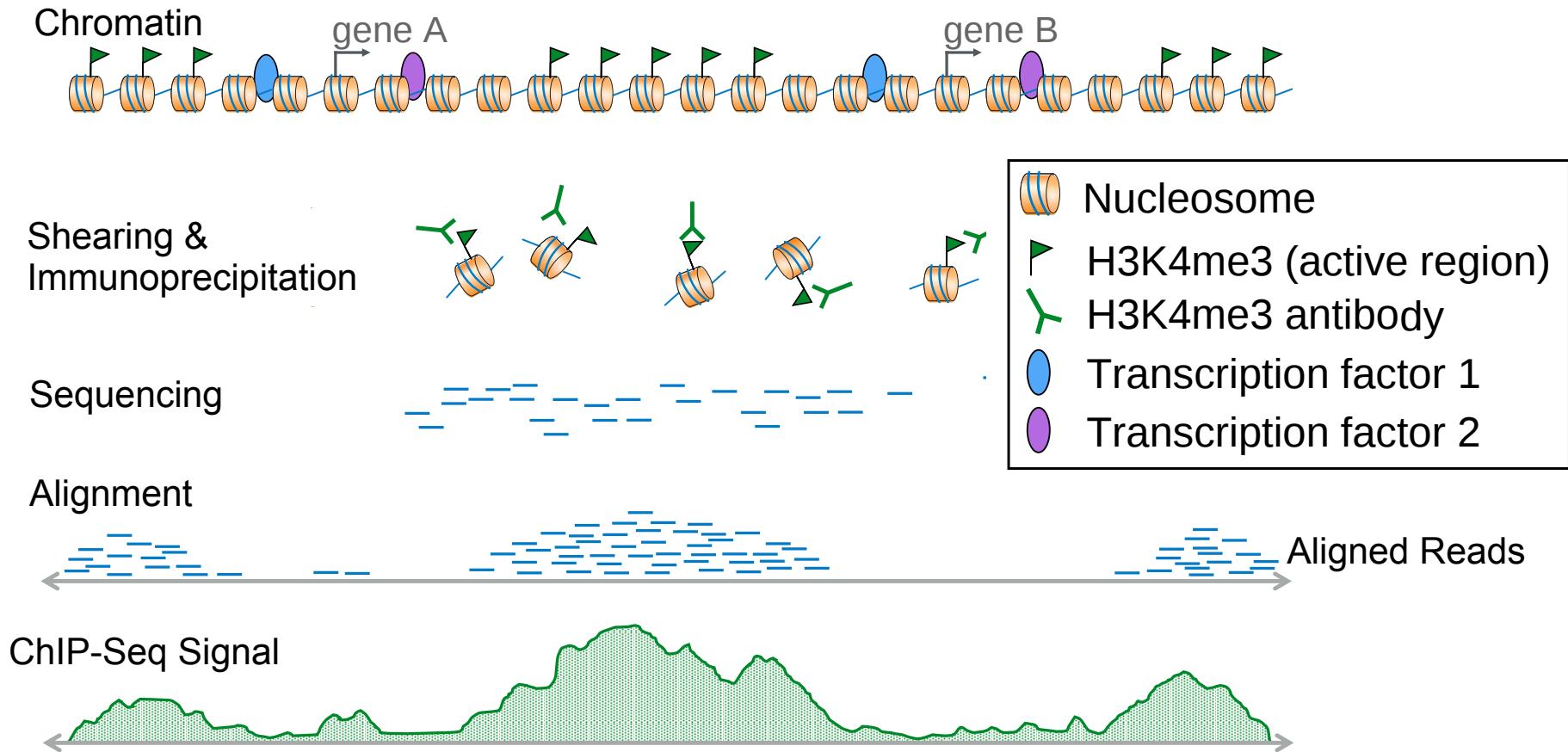
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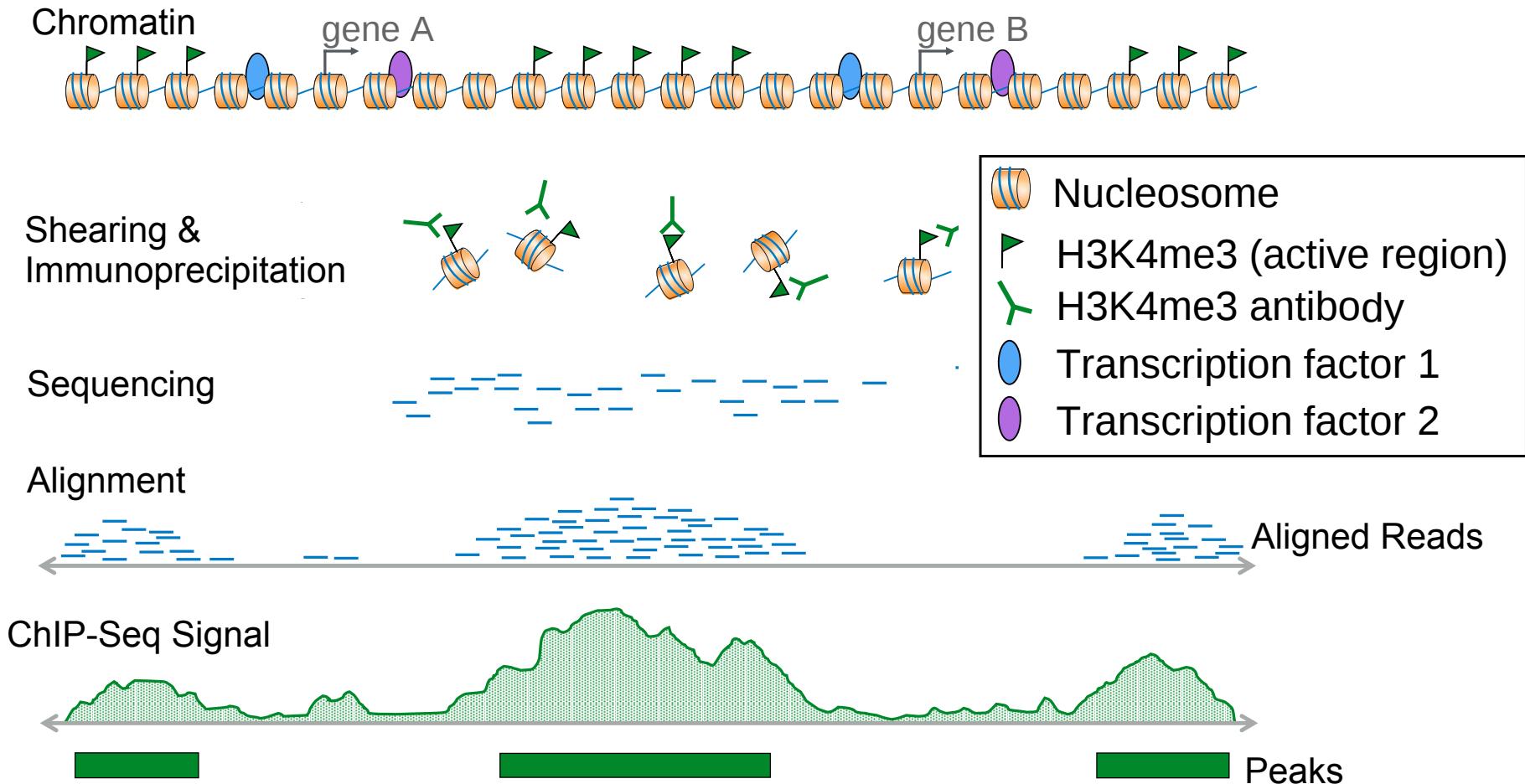
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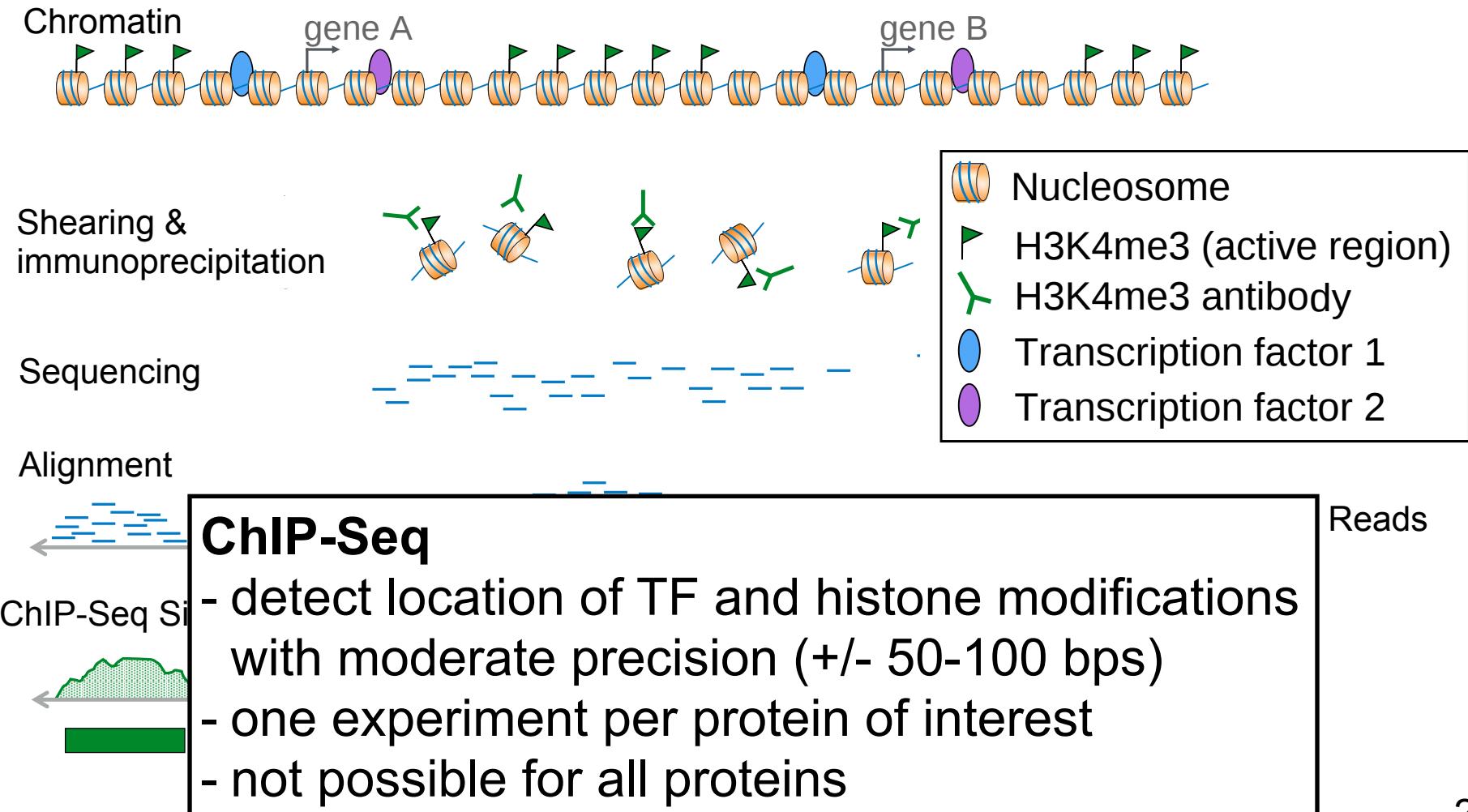
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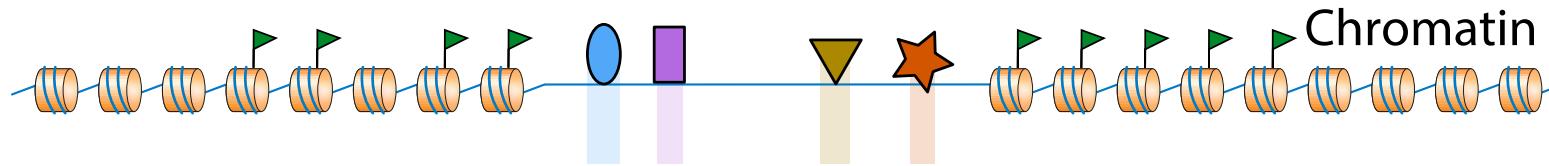
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DNA - Protein interactions with ChIP-Seq

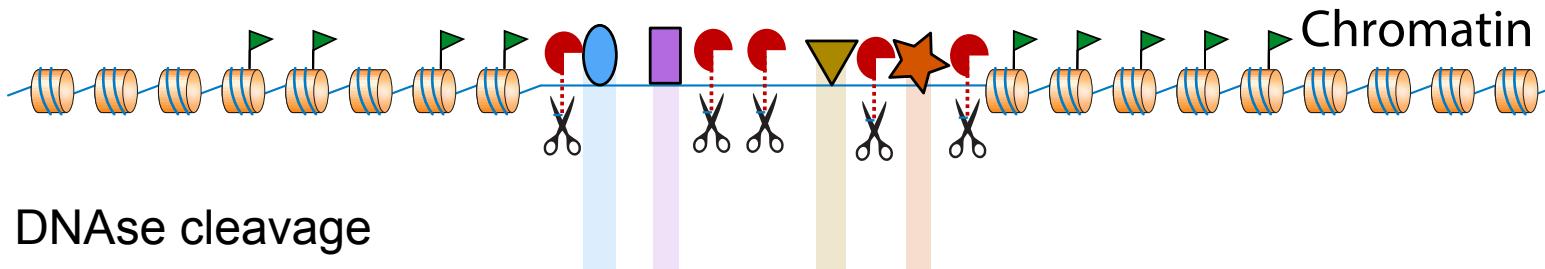


DNA - Protein interactions with DNase-Seq



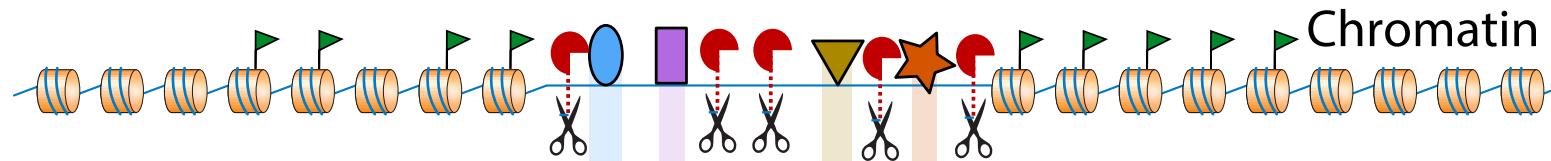
- Nucleosome
- H3K4me3
- DNase I
- Transcription Factors

DNA - Protein interactions with DNase-Seq

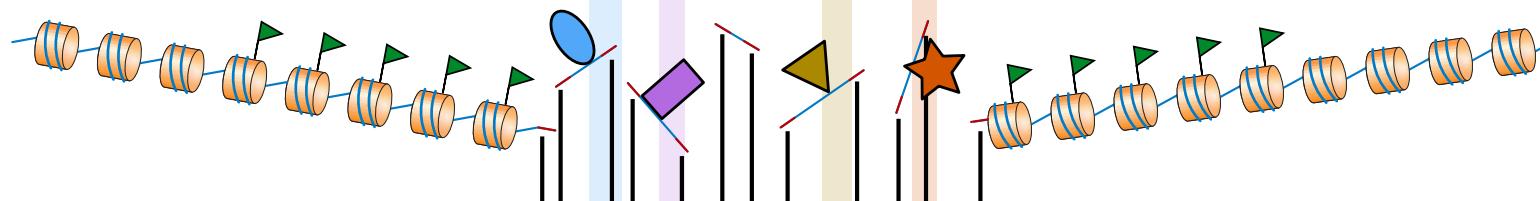


-  Nucleosome
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DNA - Protein interactions with DNase-Seq

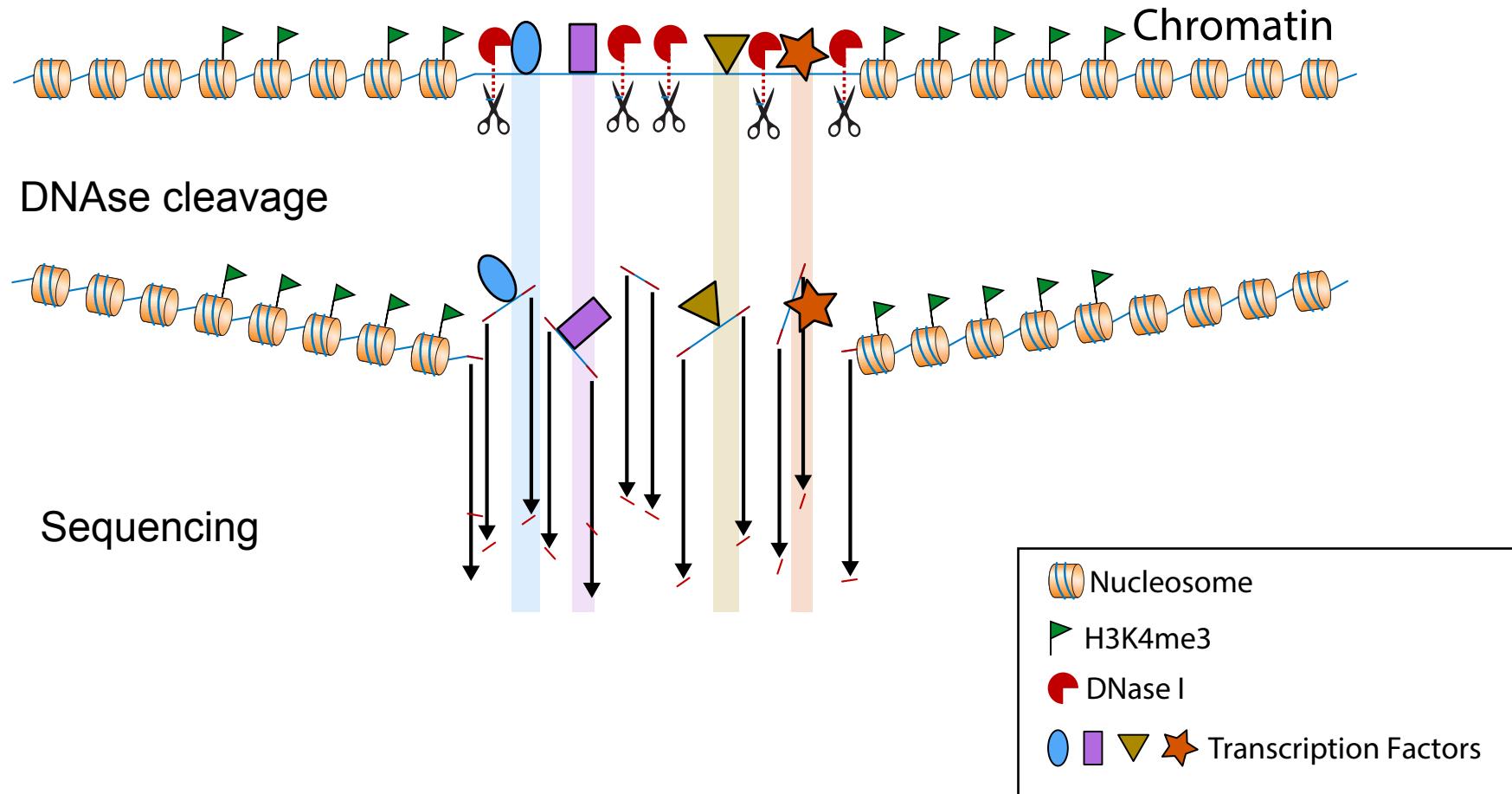


DNAse cleavage

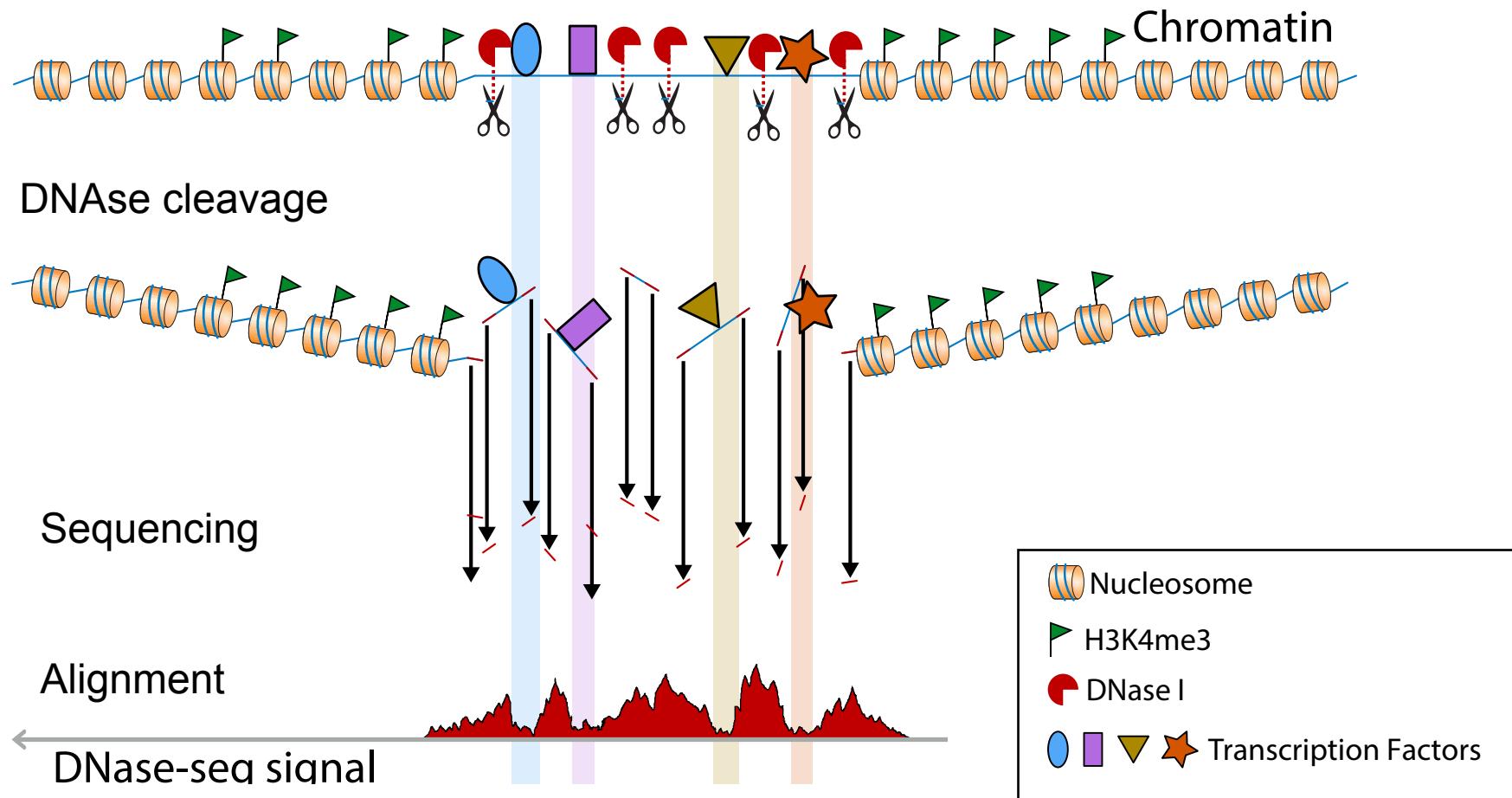


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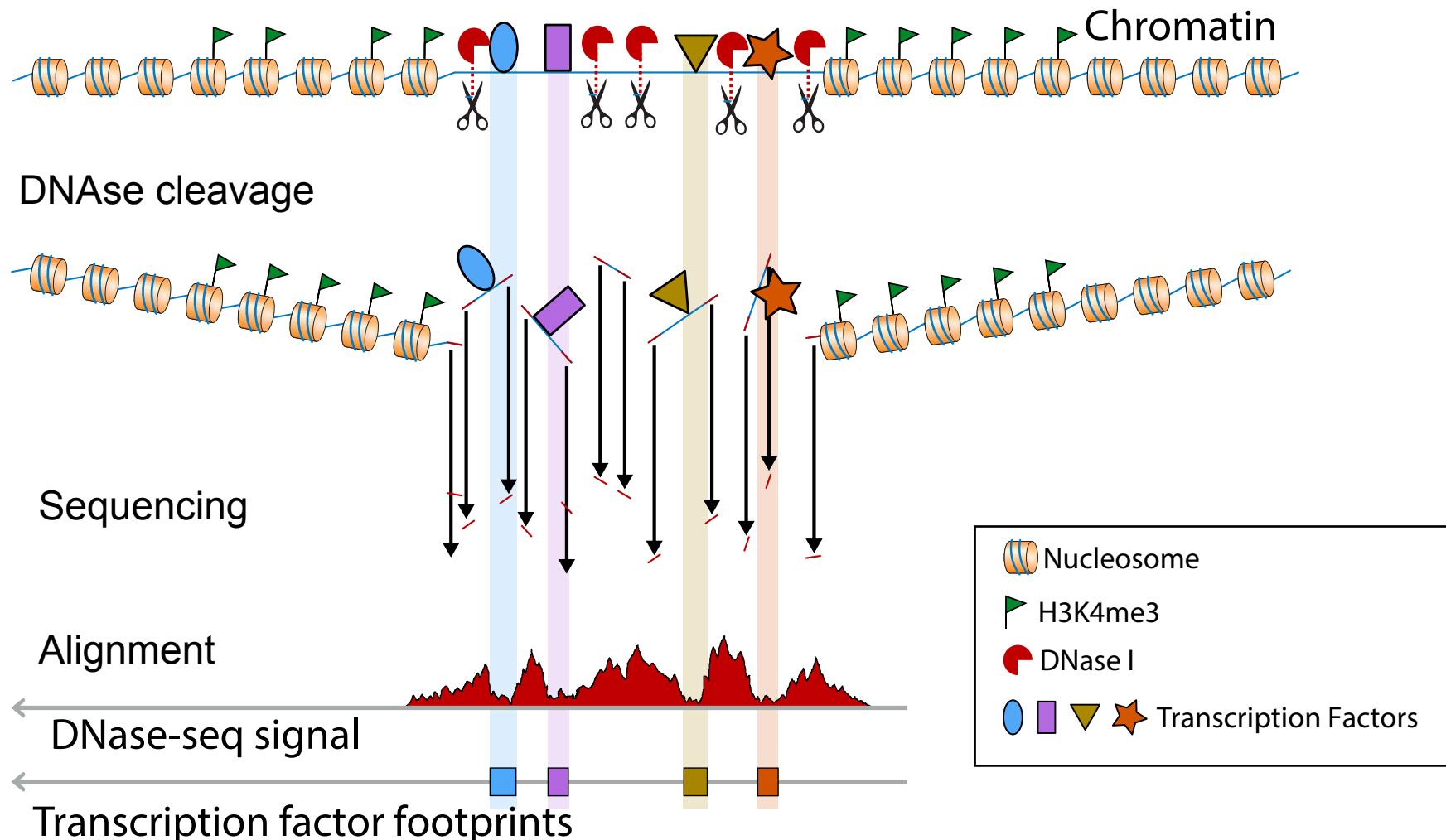
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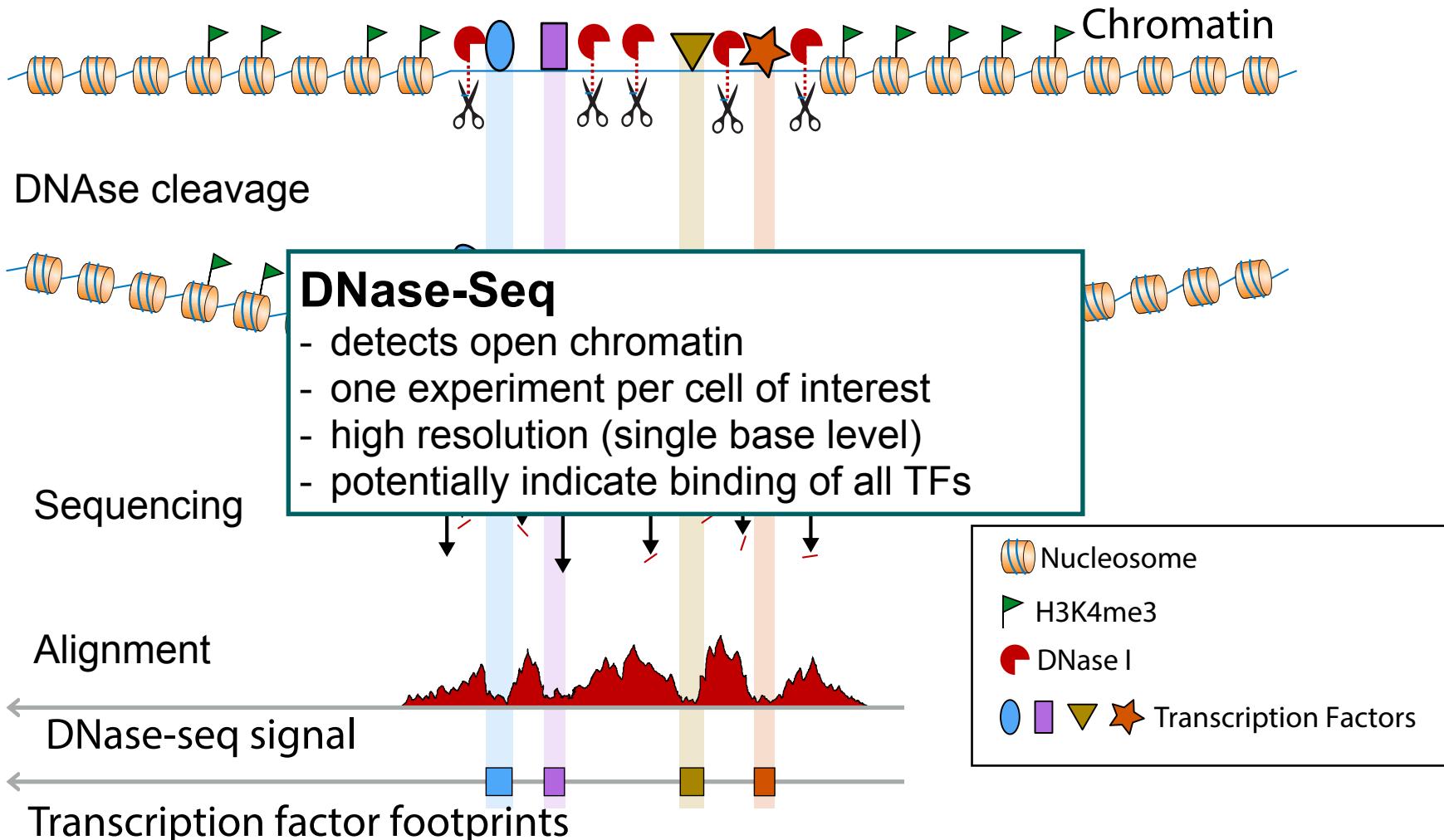
DNA - Protein interactions with DNase-Seq



DNA - Protein interactions with DNase-Seq



DNA - Protein interactions with DNase-Seq



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)

Next

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IZKF Interdisziplinäres
Zentrum für
Klinische Forschung

RWTHAACHEN
UNIVERSITY