

Prediction of Regulatory Networks from Expression and Chromatin Data

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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 (JH)



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Florian Schmidt (FS)

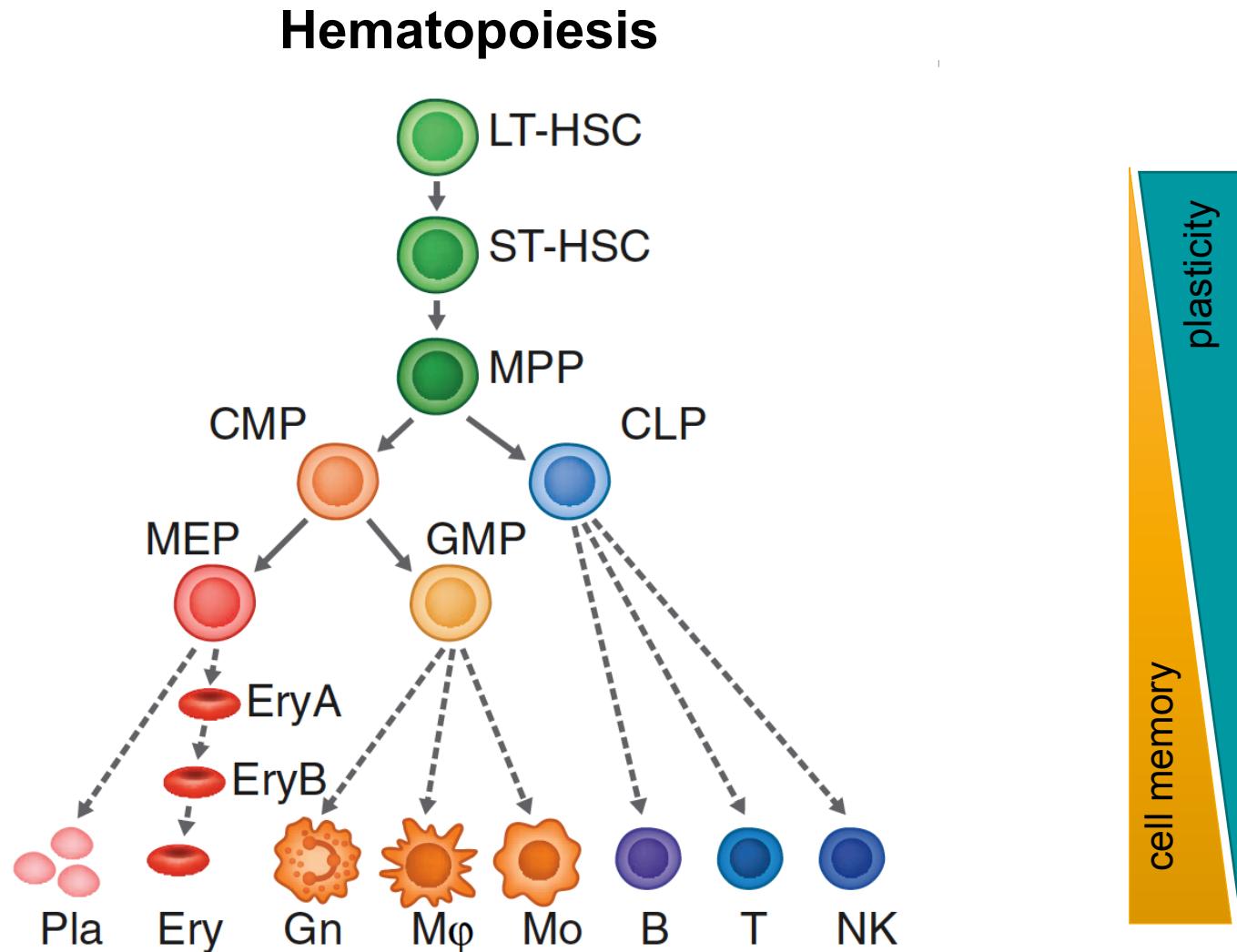
Introduction - Gene Regulation, Transcription and Chromatin

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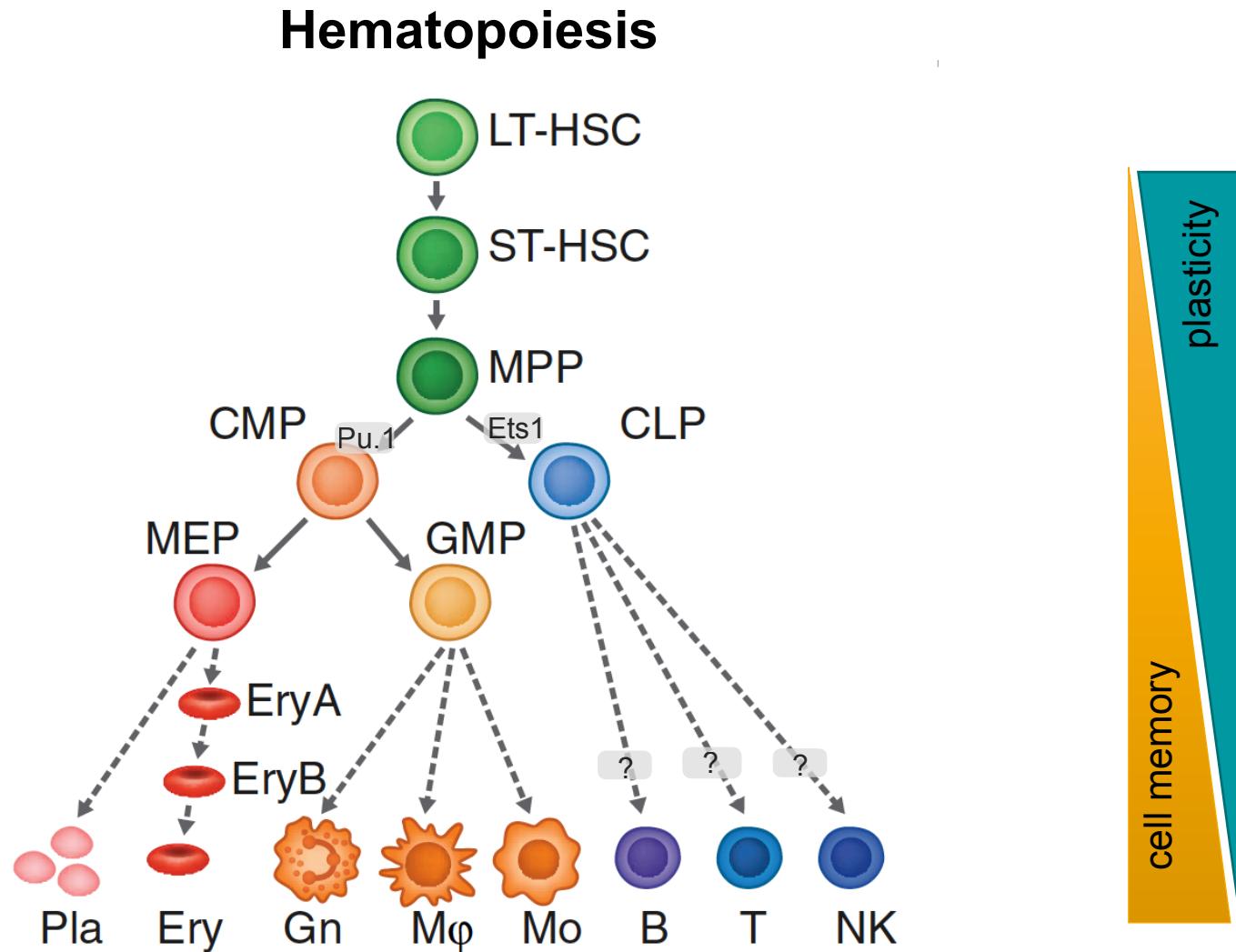


Cell Differentiation & Gene Regulation



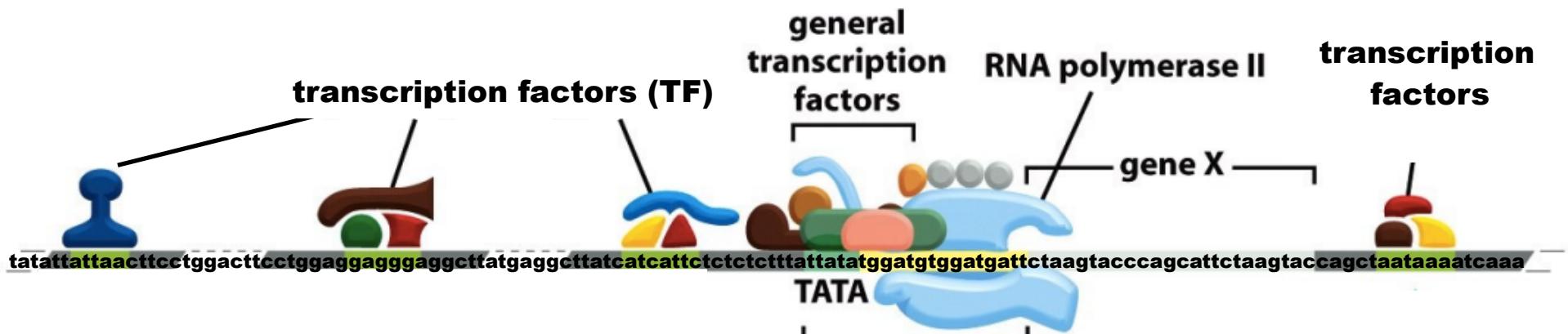
Adapted from Lara-Astiaso, Science, 2015.

Cell Differentiation & Gene Regulation

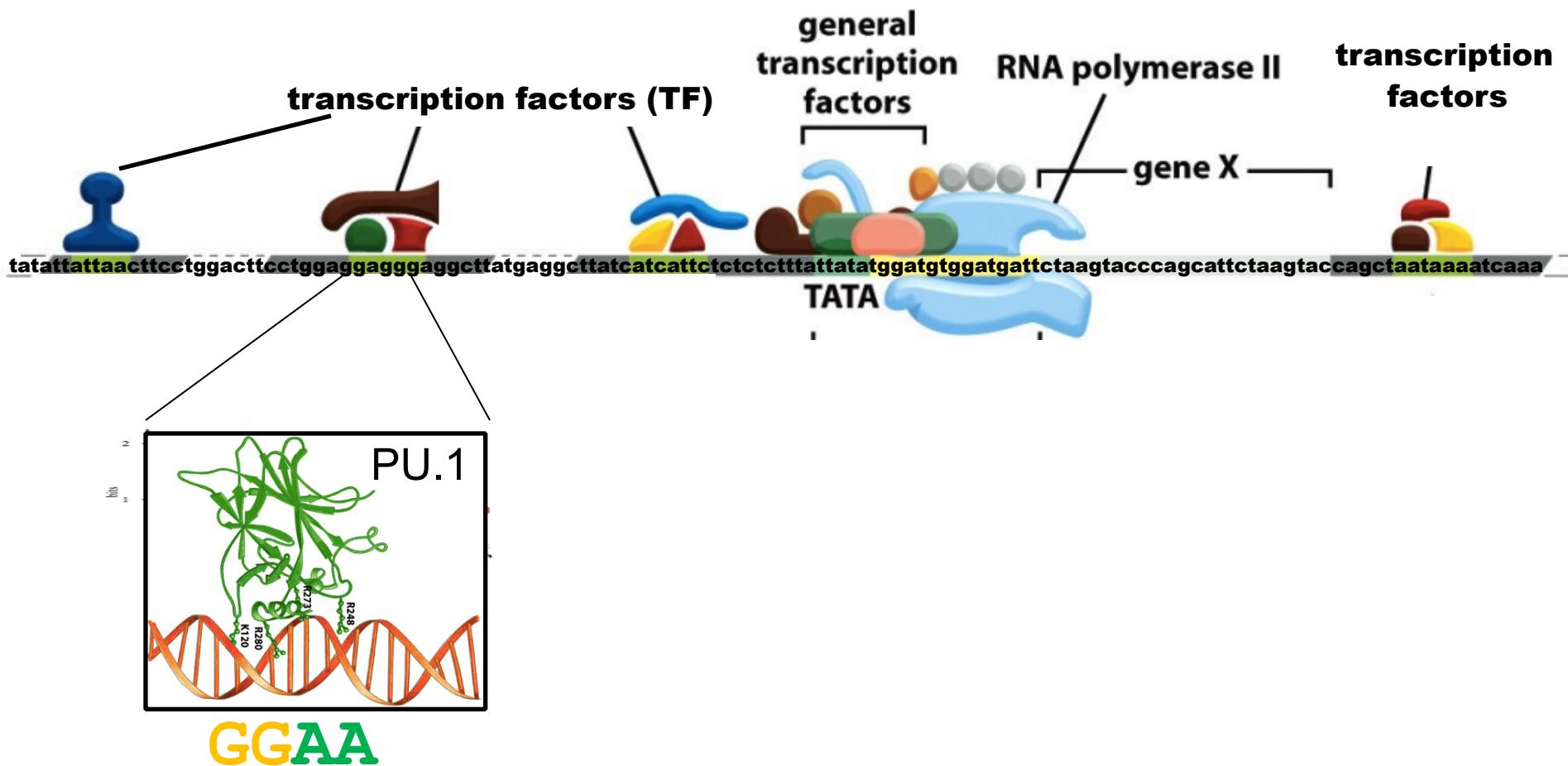


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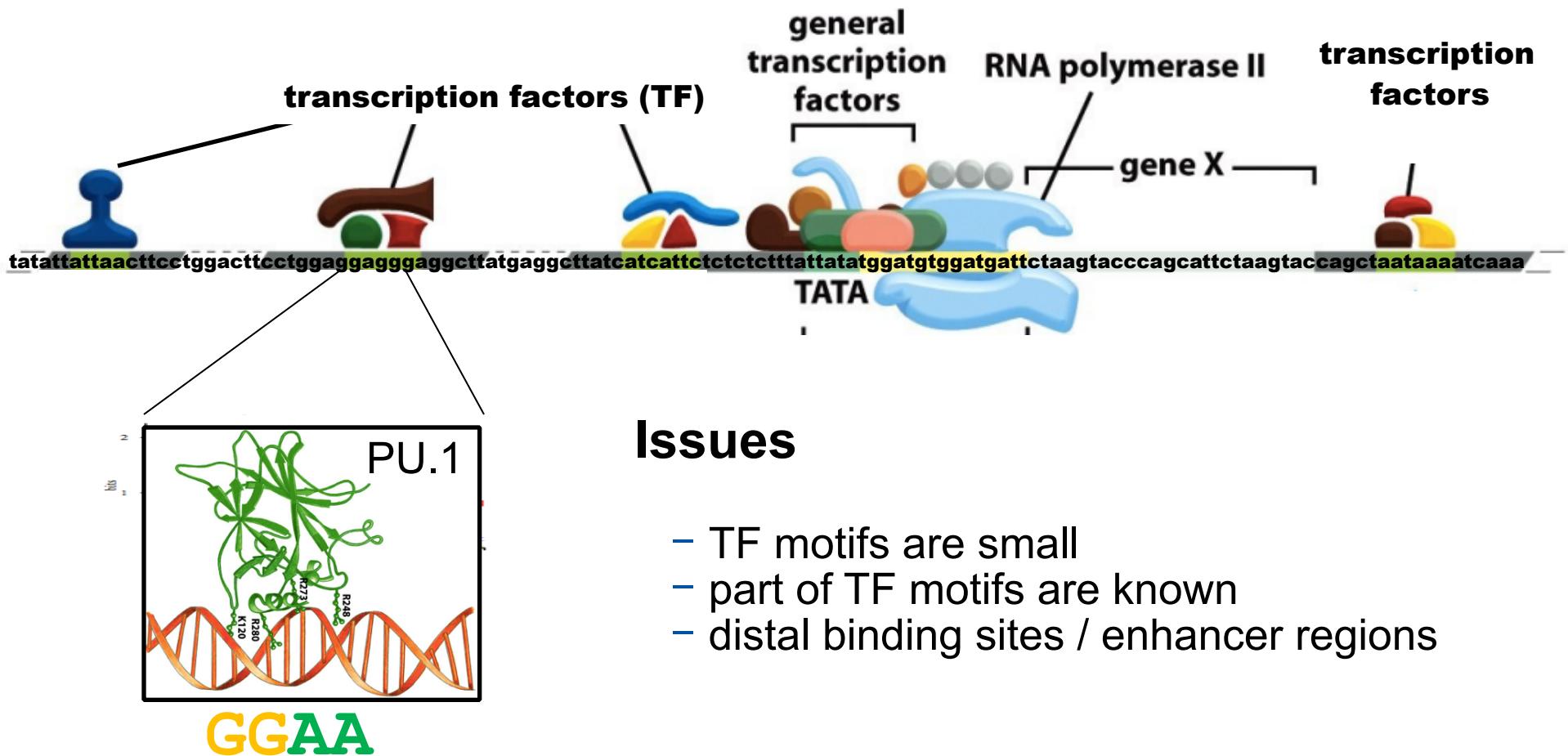
Regulatory Control – Protein-DNA interaction



Regulatory Control – Protein-DNA interaction



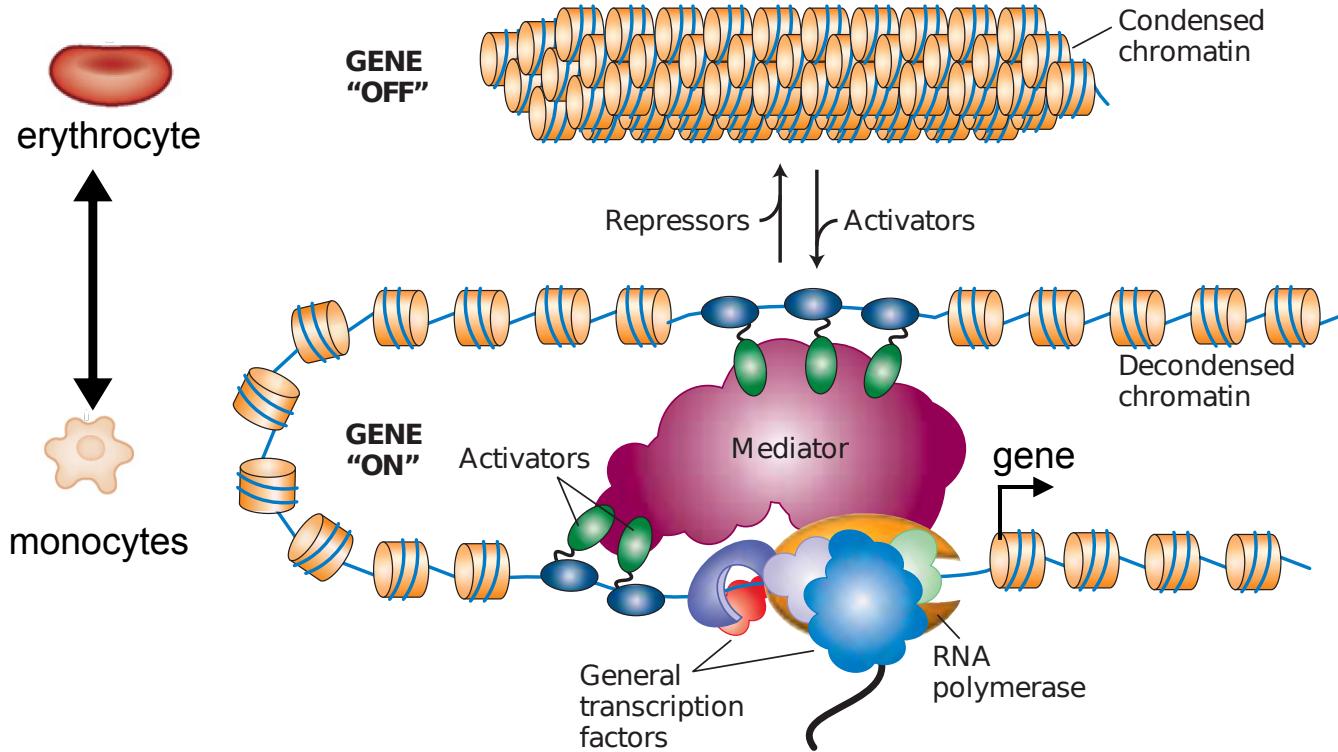
Regulatory Control – Protein-DNA interaction



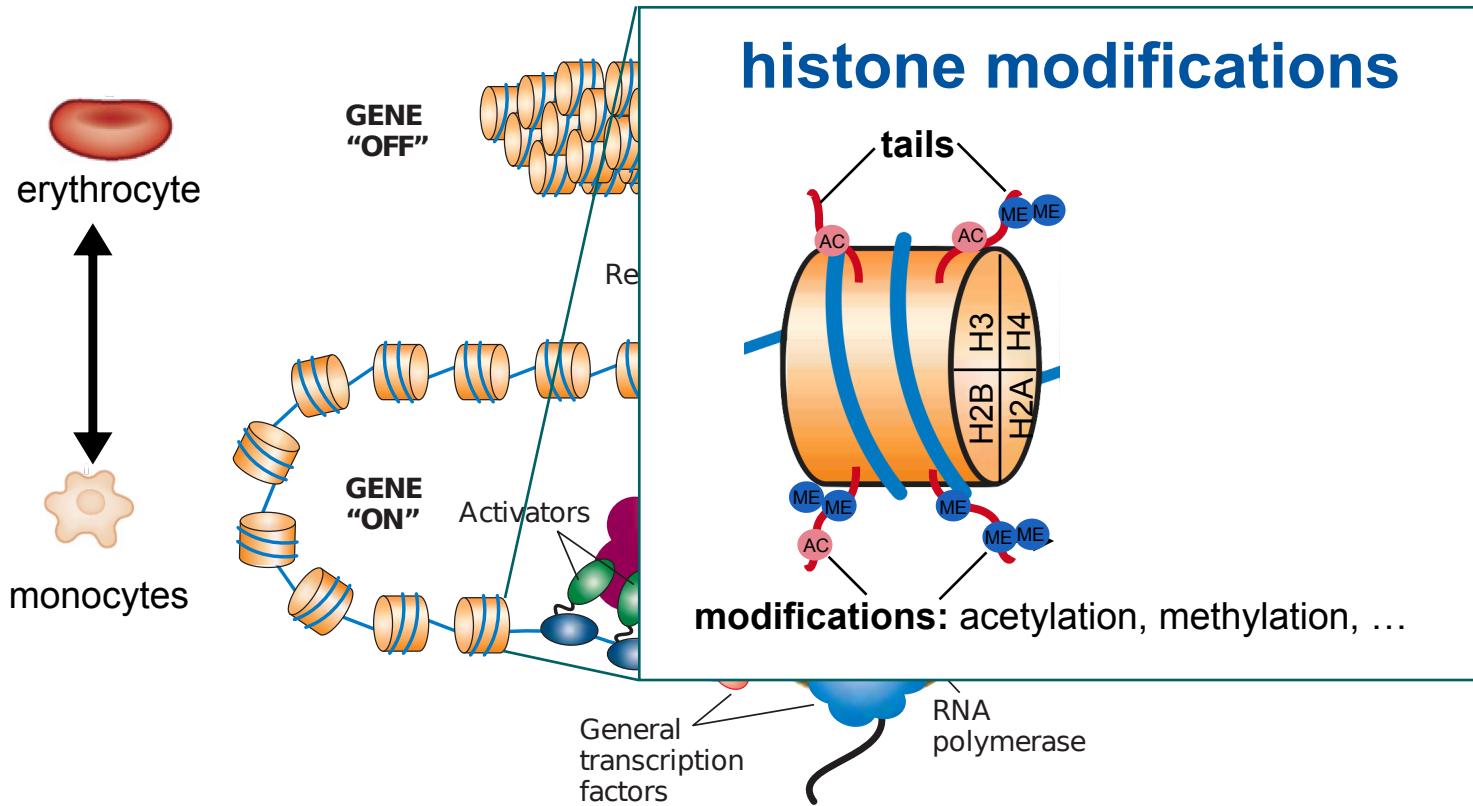
Issues

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

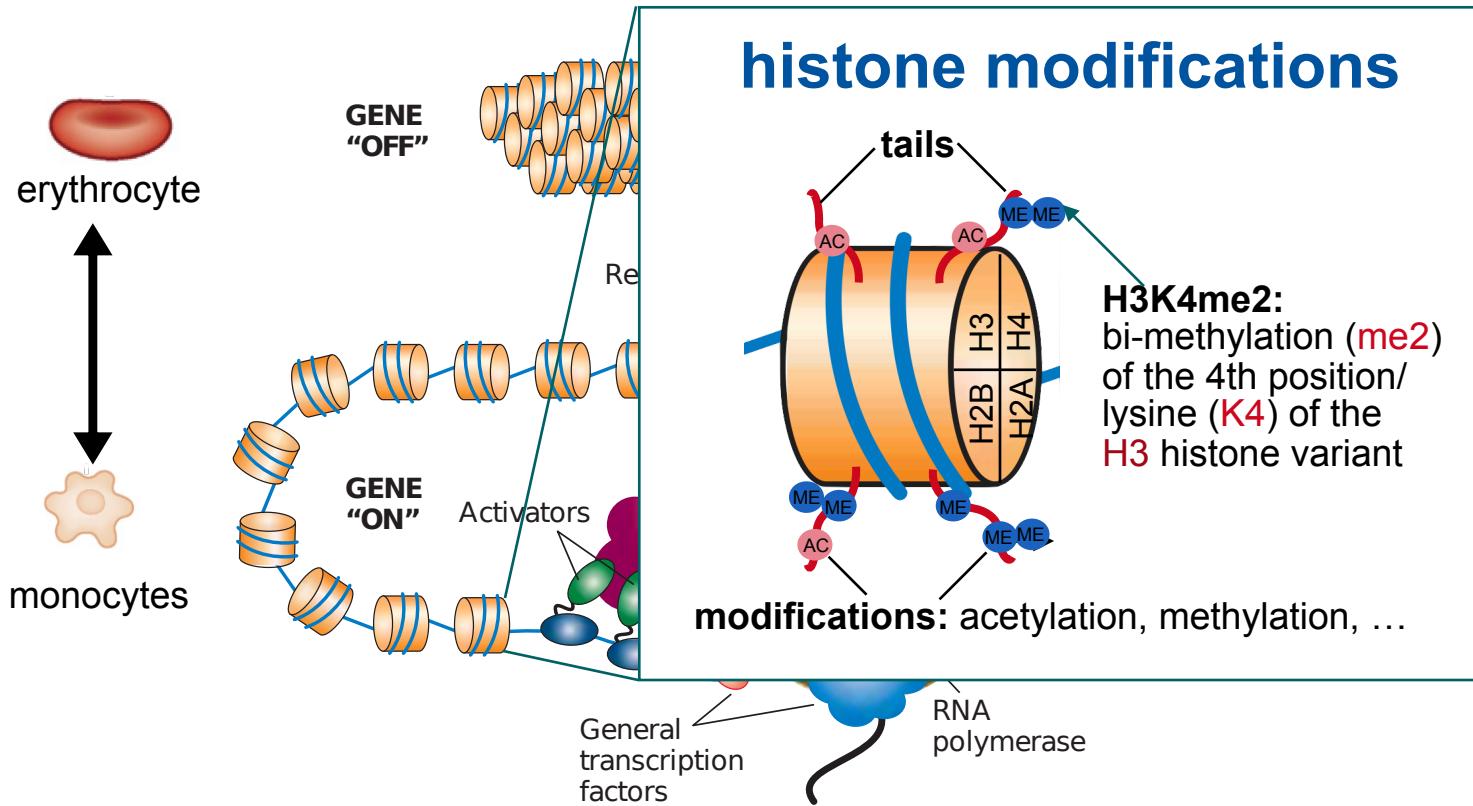
Chromatin and Cell Memory/Plasticity



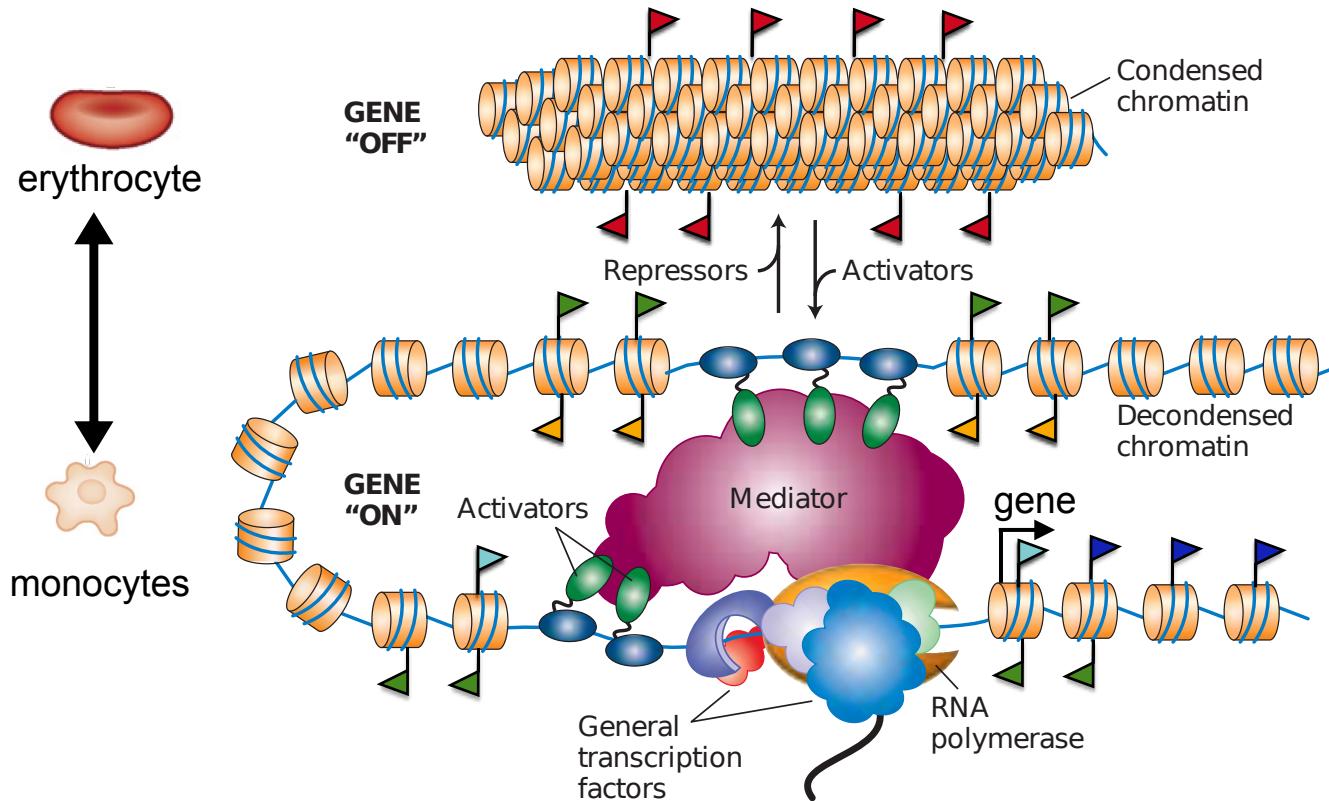
Chromatin and Histones



Chromatin and Histones



Chromatin and Cell Memory/Plasticity



Histone Code

► Transcription

H3K79me2, H3k36me3

► Active Regions

H3K27ac, H3K9ac

► Active Promoters

H3K4me3

► Active Enhancers

H3K4me1

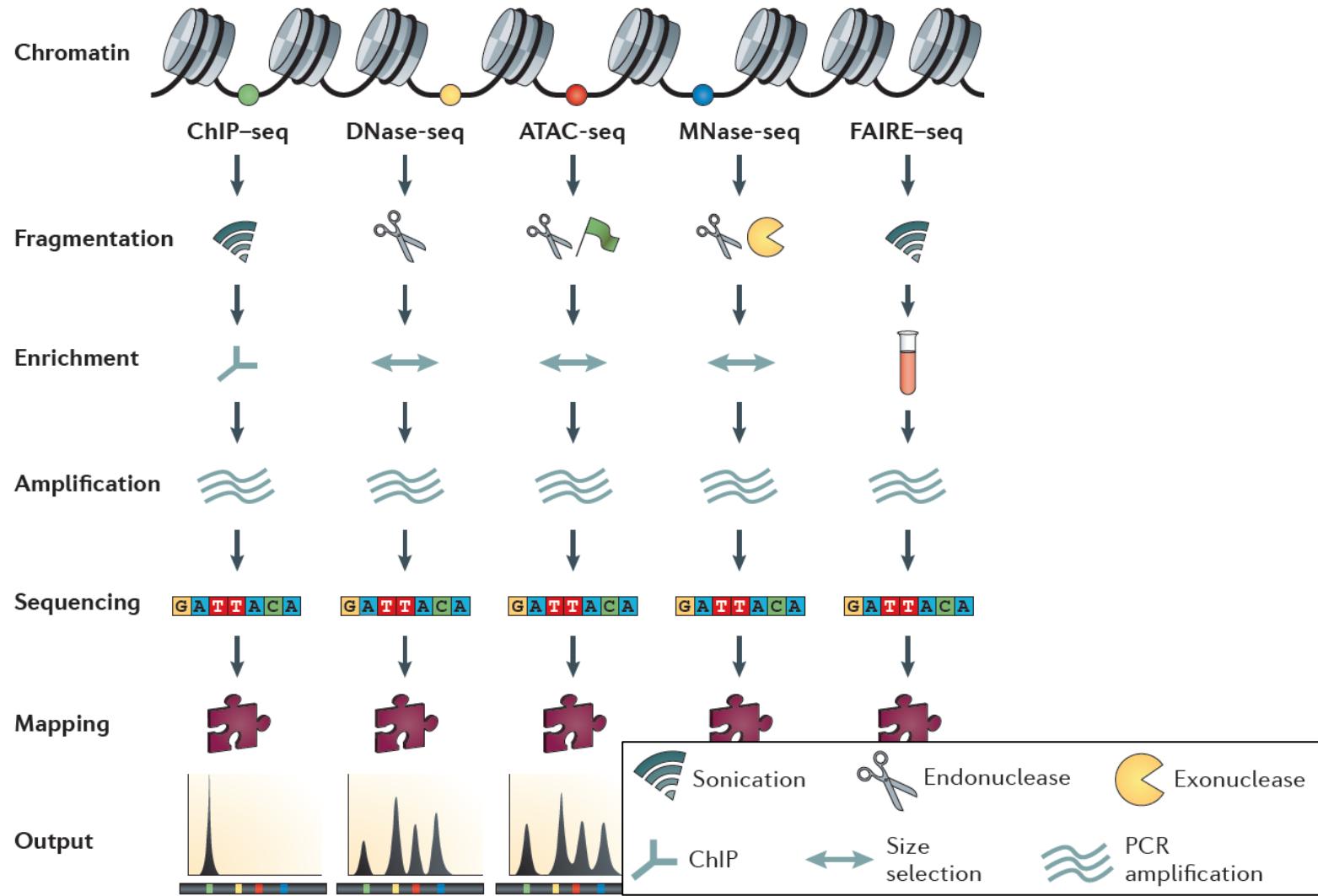
► Repressed Prom.

H3K27me3

► Repressed Regions

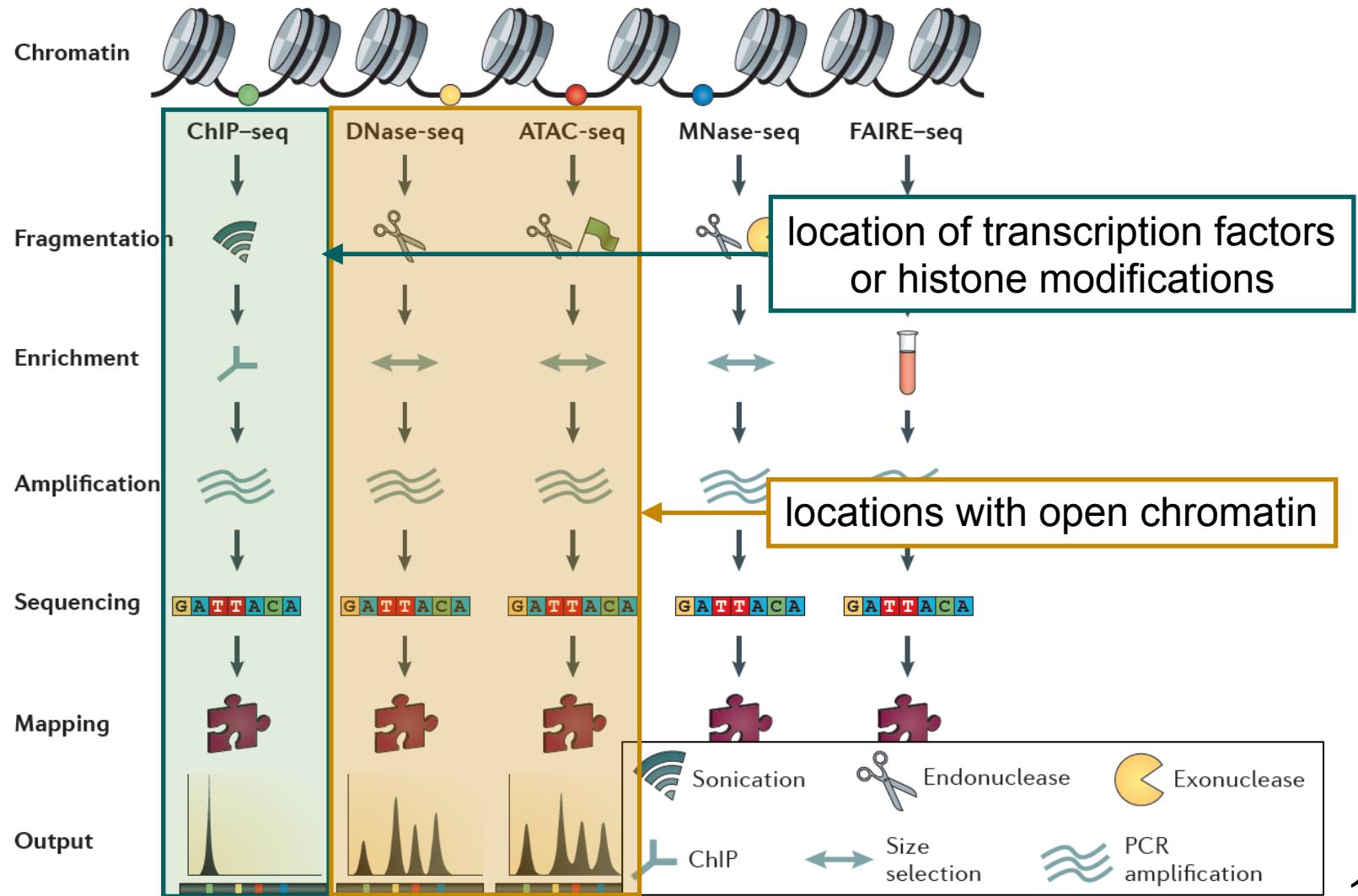
H3K9me3

NGS and Chromatin



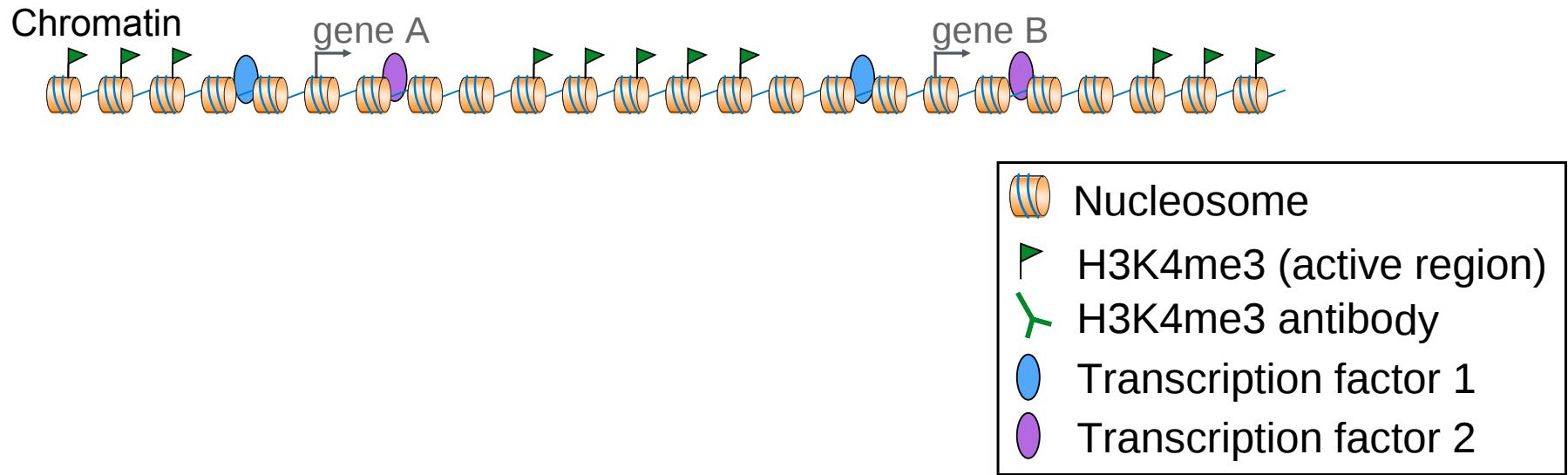
Source: Meyer, C.A. and Liu X.S. (2014). *Nature Reviews Genetics*.

NGS and Chromatin

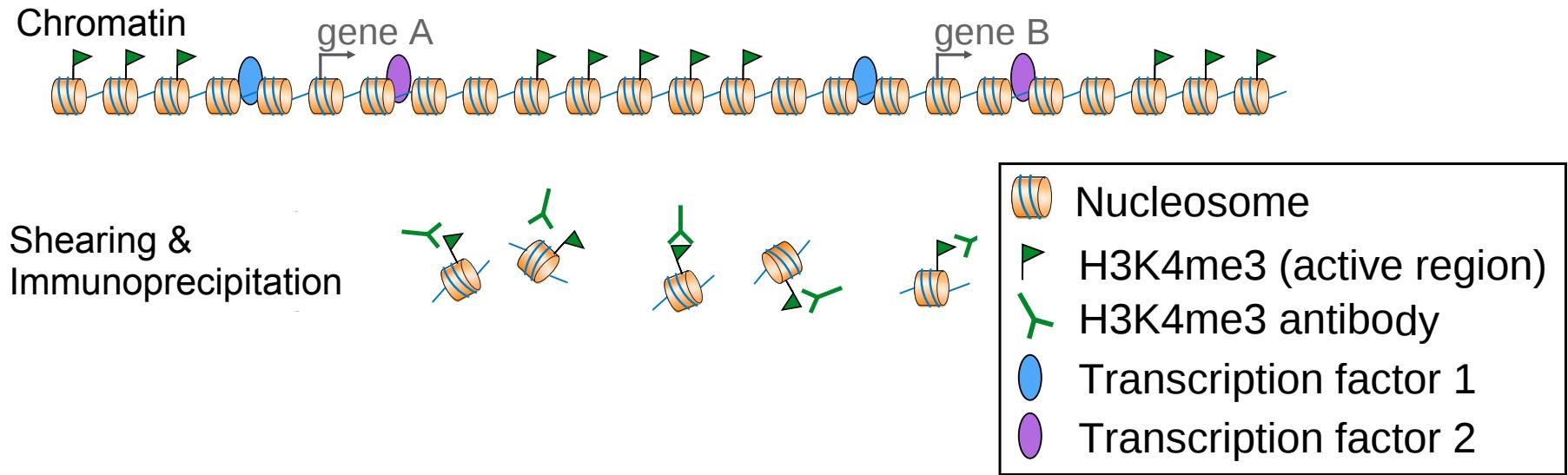


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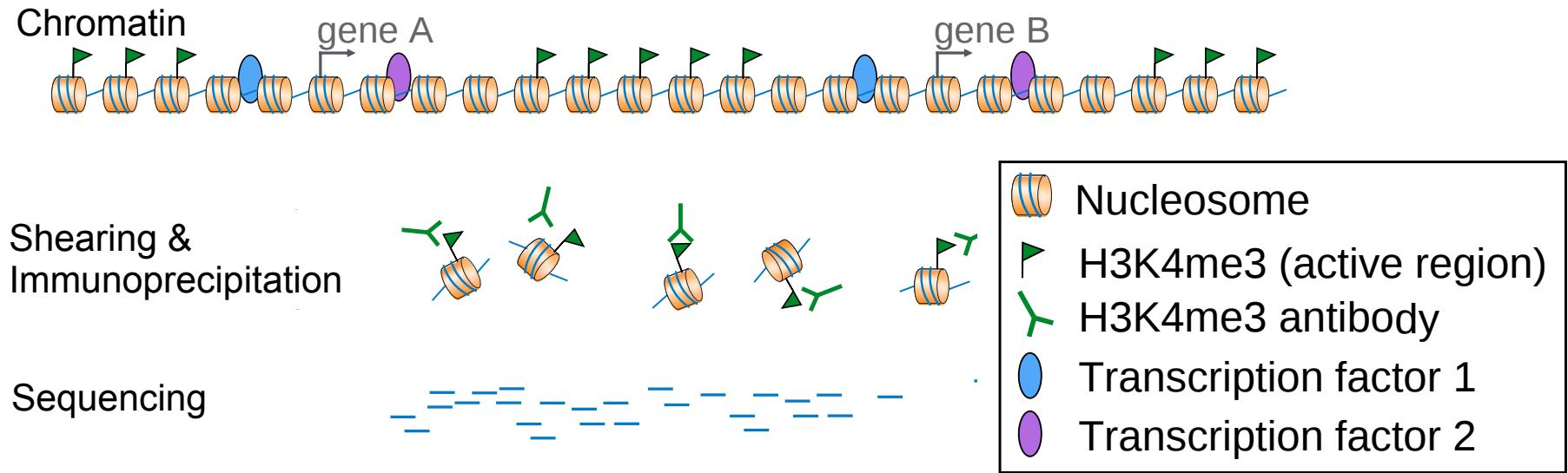
DNA - Protein interactions with ChIP-Seq



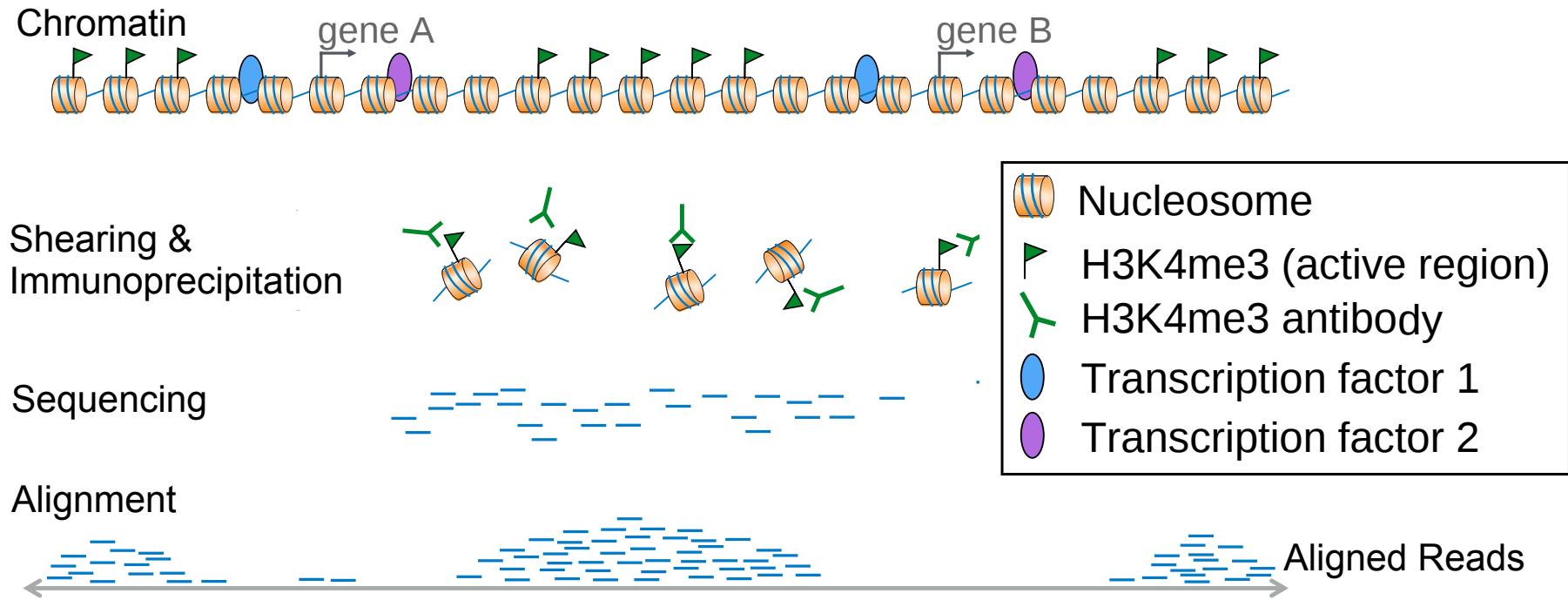
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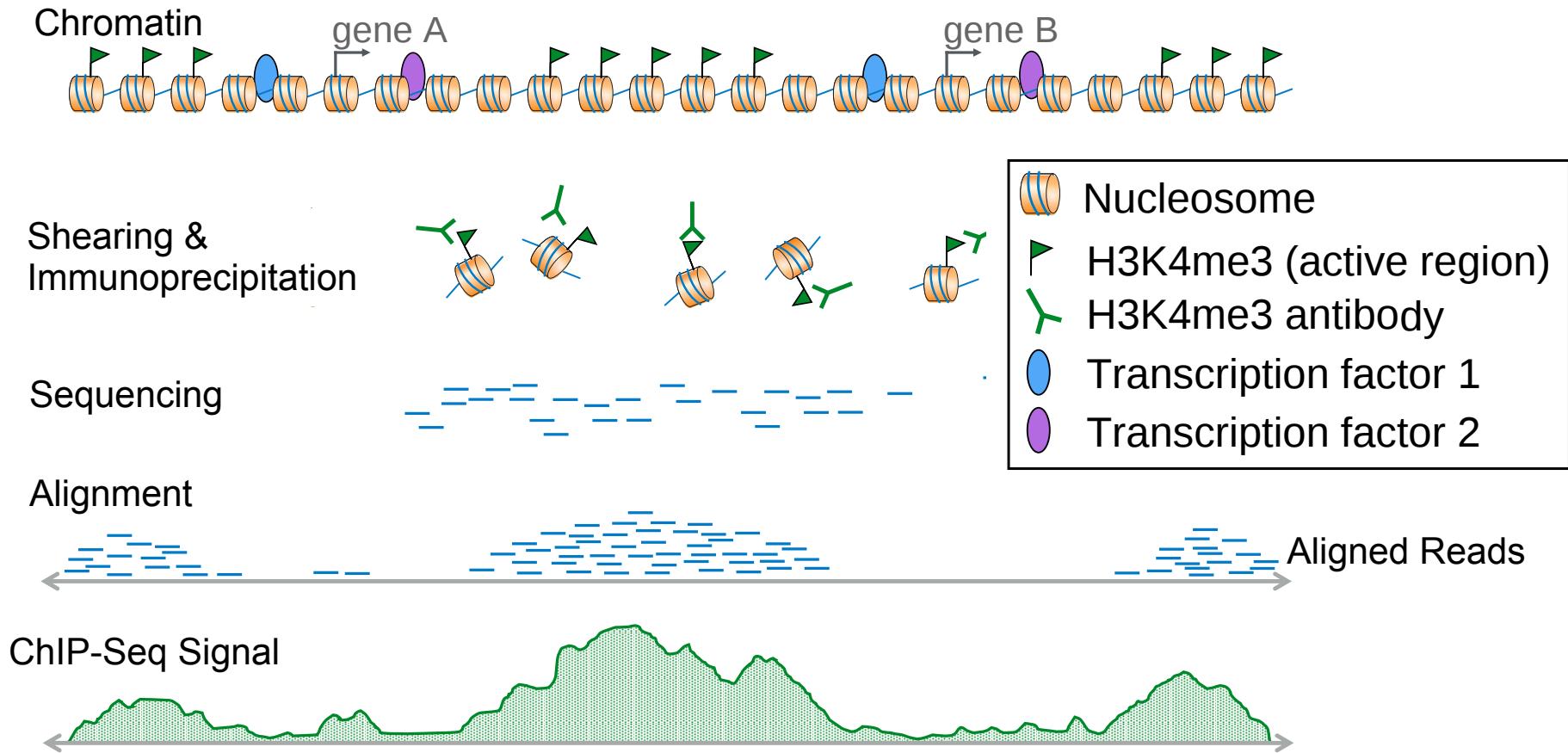
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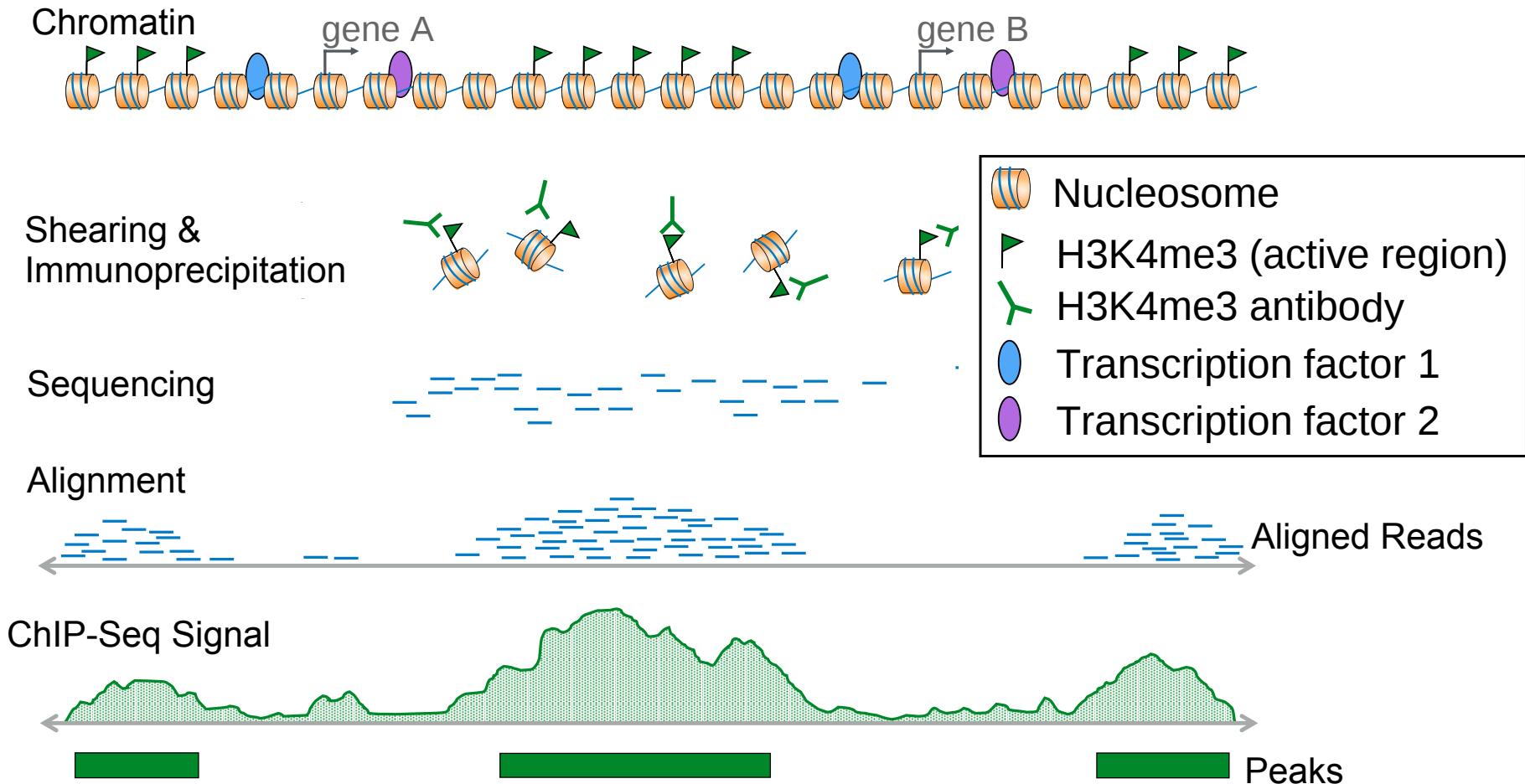
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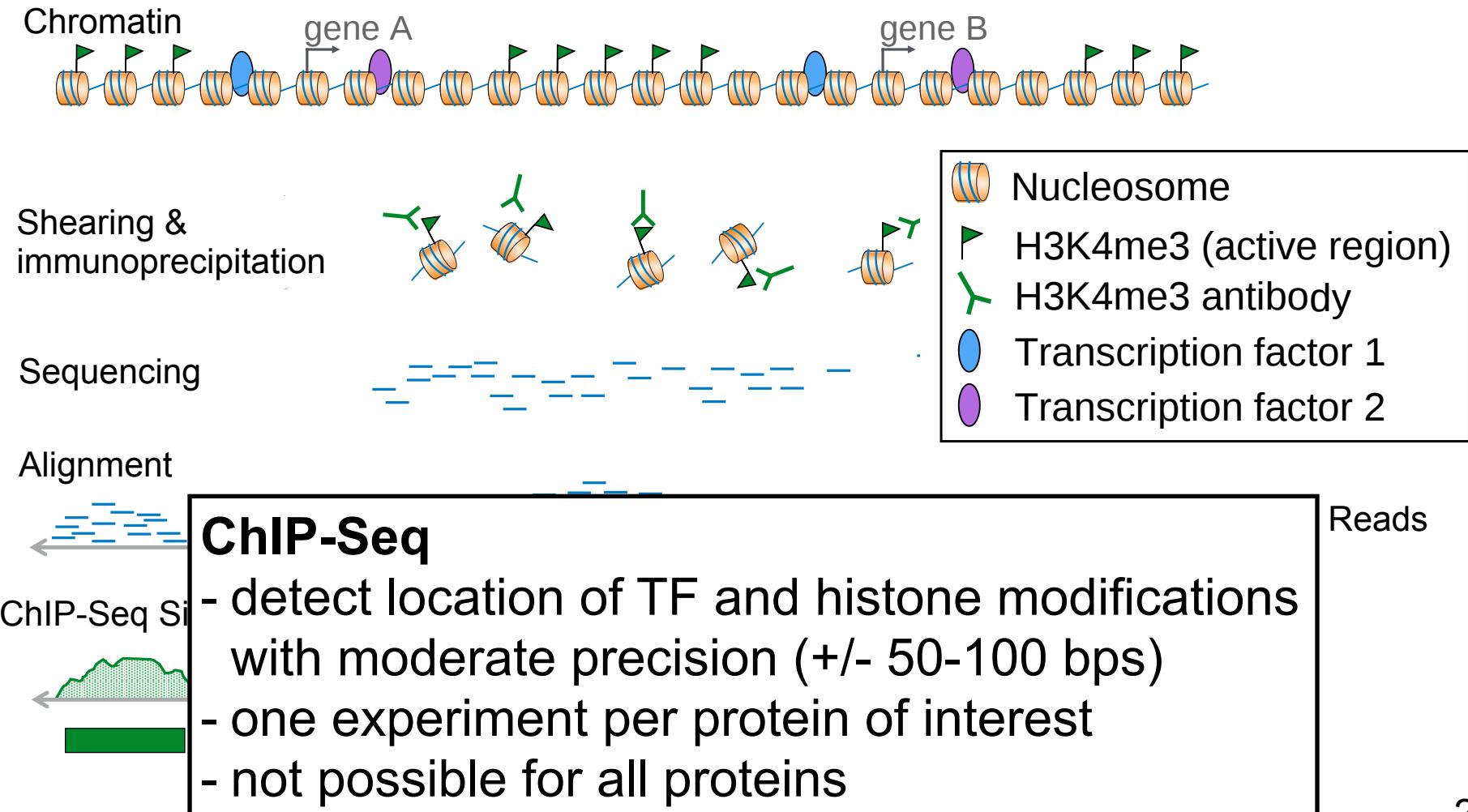
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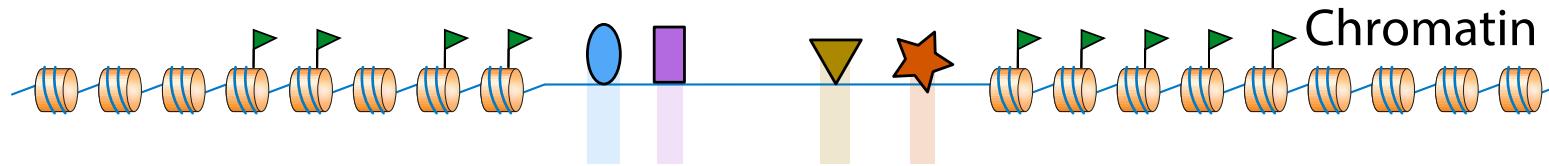
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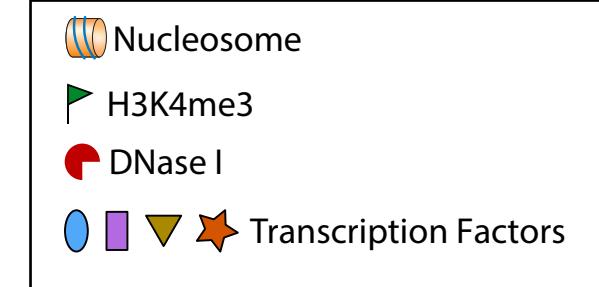
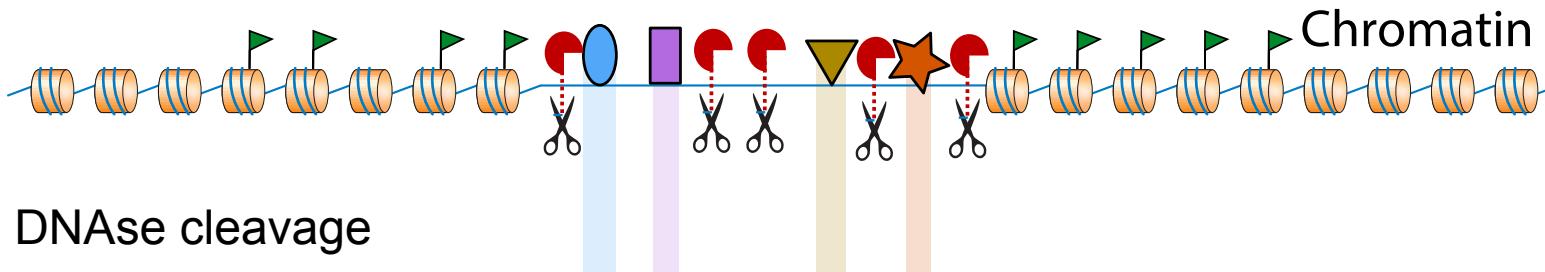


DNA - Protein interactions with DNase-Seq

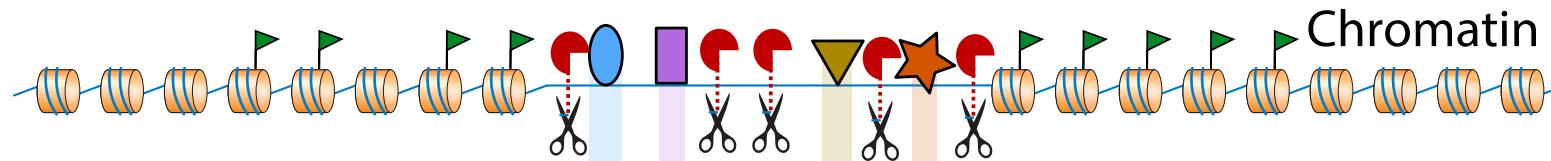


- Nucleosome
- H3K4me3
- DNase I
- Transcription Factors

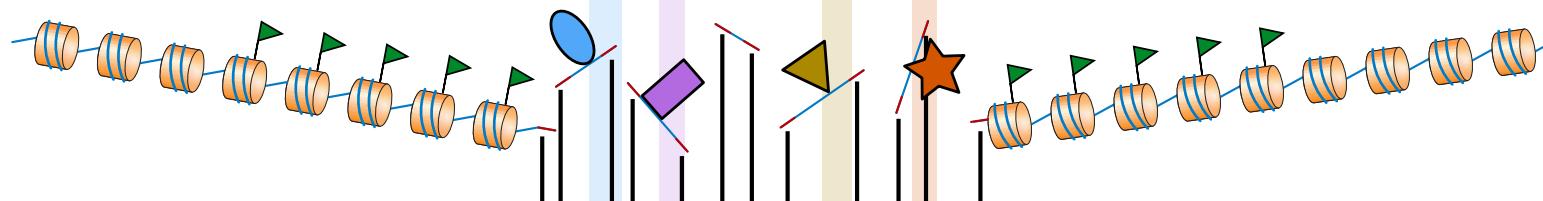
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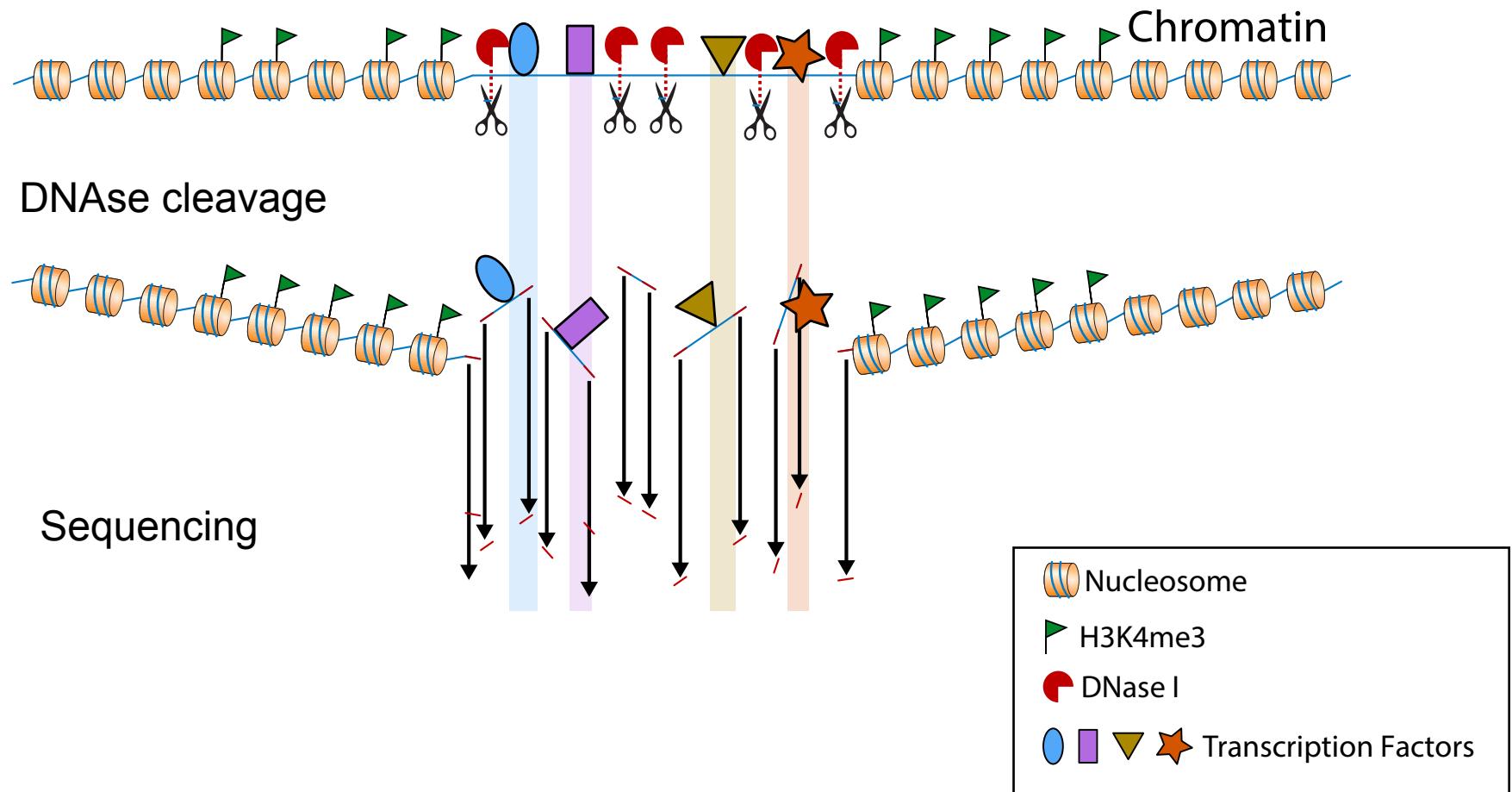


DNAse cleavage

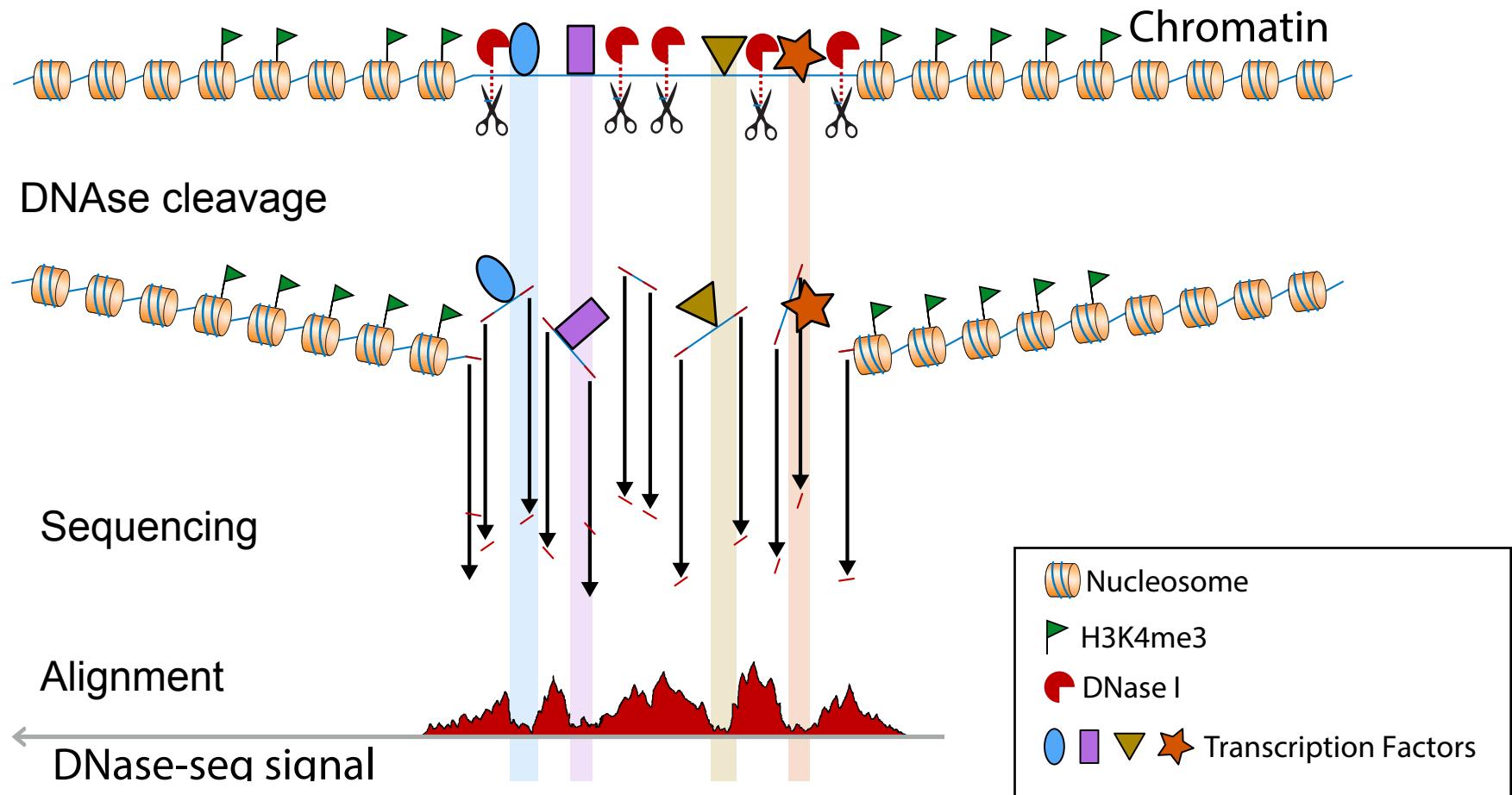


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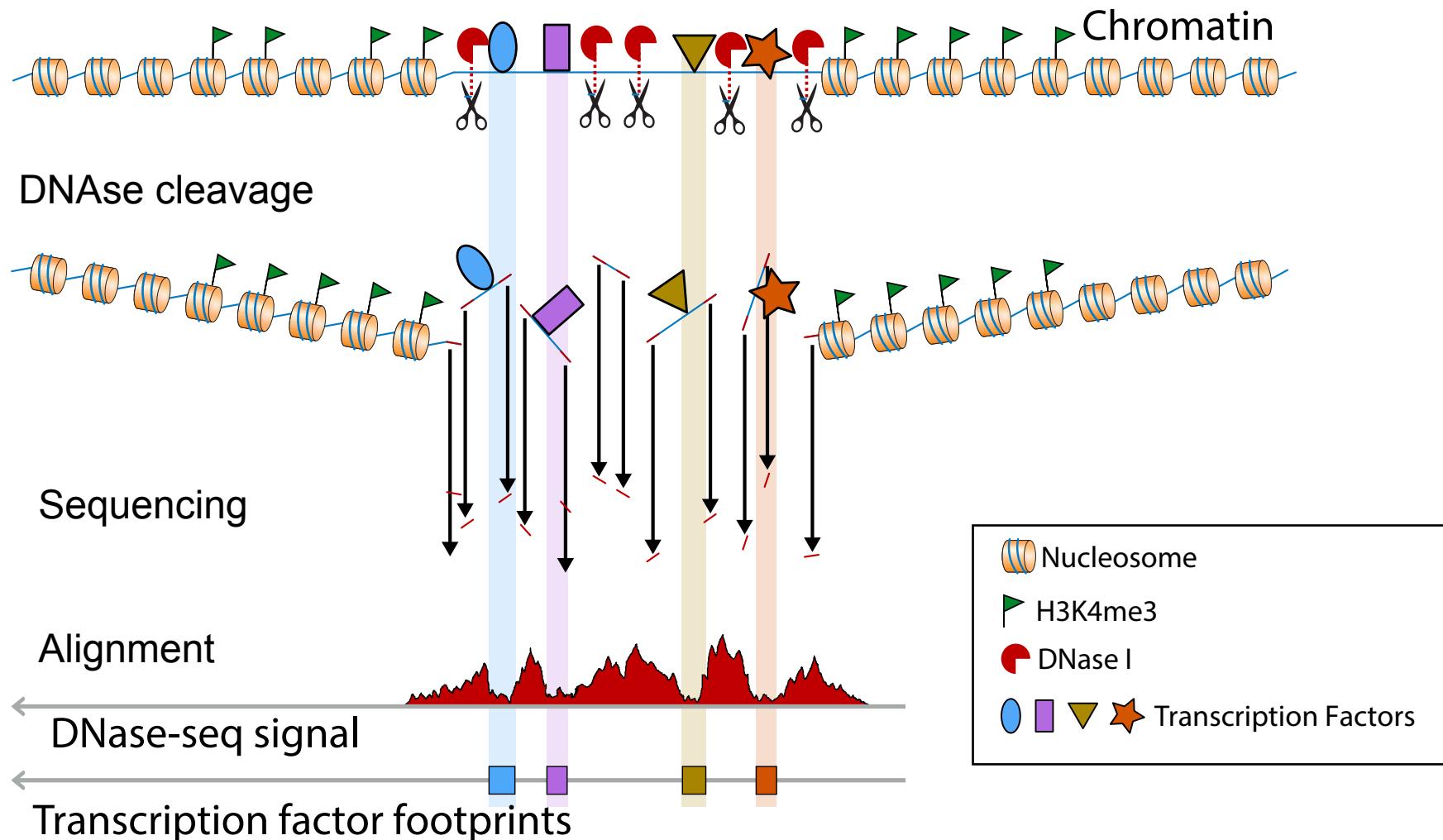
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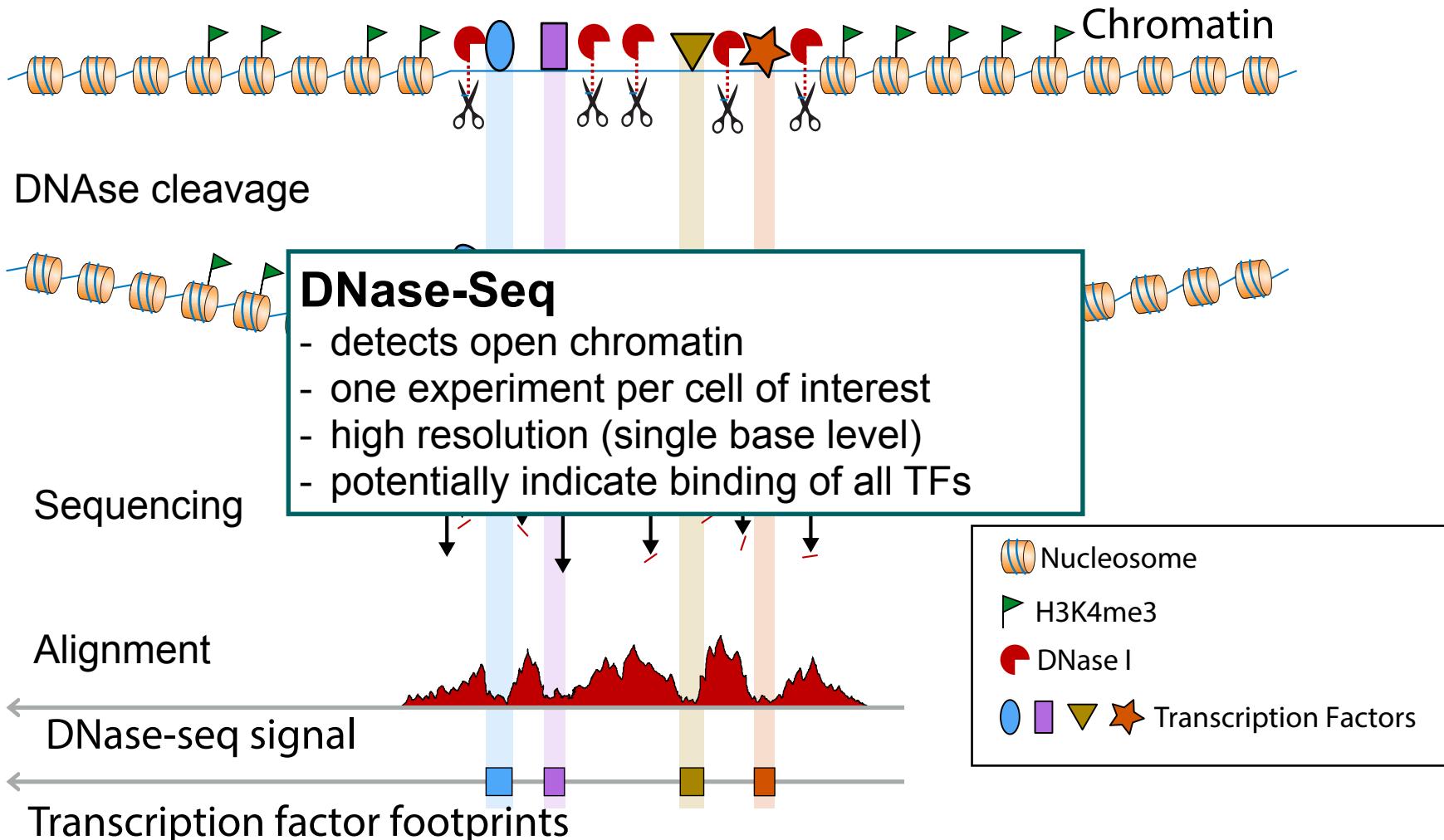
DNA - Protein interactions with DNase-Seq



DNA - Protein interactions with DNase-Seq



DNA - Protein interactions with DNase-Seq



Summary

Transcription factors

- main player of gene regulation/transcription

Chromatin

- controls cellular memory/plasticity

Histone modifications

- indicate regulatory status of genomic regions

Next generation sequencing

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

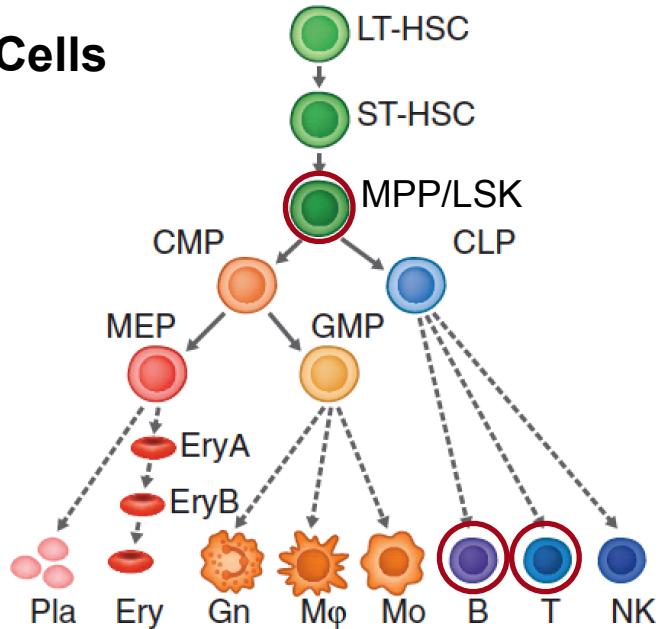
Tutorial - Prediction of Regulatory Networks

Learning Objectives

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

Tutorial - Prediction of Regulatory Networks

Cells



Questions:

- 1 - Which regions have chromatin changes in selected cells?
- 2 - What are the cell specific binding sites?
- 3 - Which transcription factors regulate expression changes?

Experiments:

RNA-seq

ATAC-seq

Chip-seq: H3K4me1, H3k4me2,
H3k4me3, H3k27ac

Source:

Chromatin state dynamics during blood formation

David Lara-Astiaso,^{1*} Assaf Weiner,^{2,3*} Erika Lorenzo-Vivas,¹ Irina Zaretsky,¹ Diego Adhemar Jaitin,¹ Eyal David,¹ Hadas Keren-Shaul,¹ Alexander Mildner,¹ Deborah Winter,¹ Steffen Jung,¹ Nir Friedman,^{2,3†} Ido Amit^{1†}

Next

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