

Assay for Transposase-Accessible Chromatin – sequencing (ATAC-seq)

Epigenomics Data Analysis Workshop

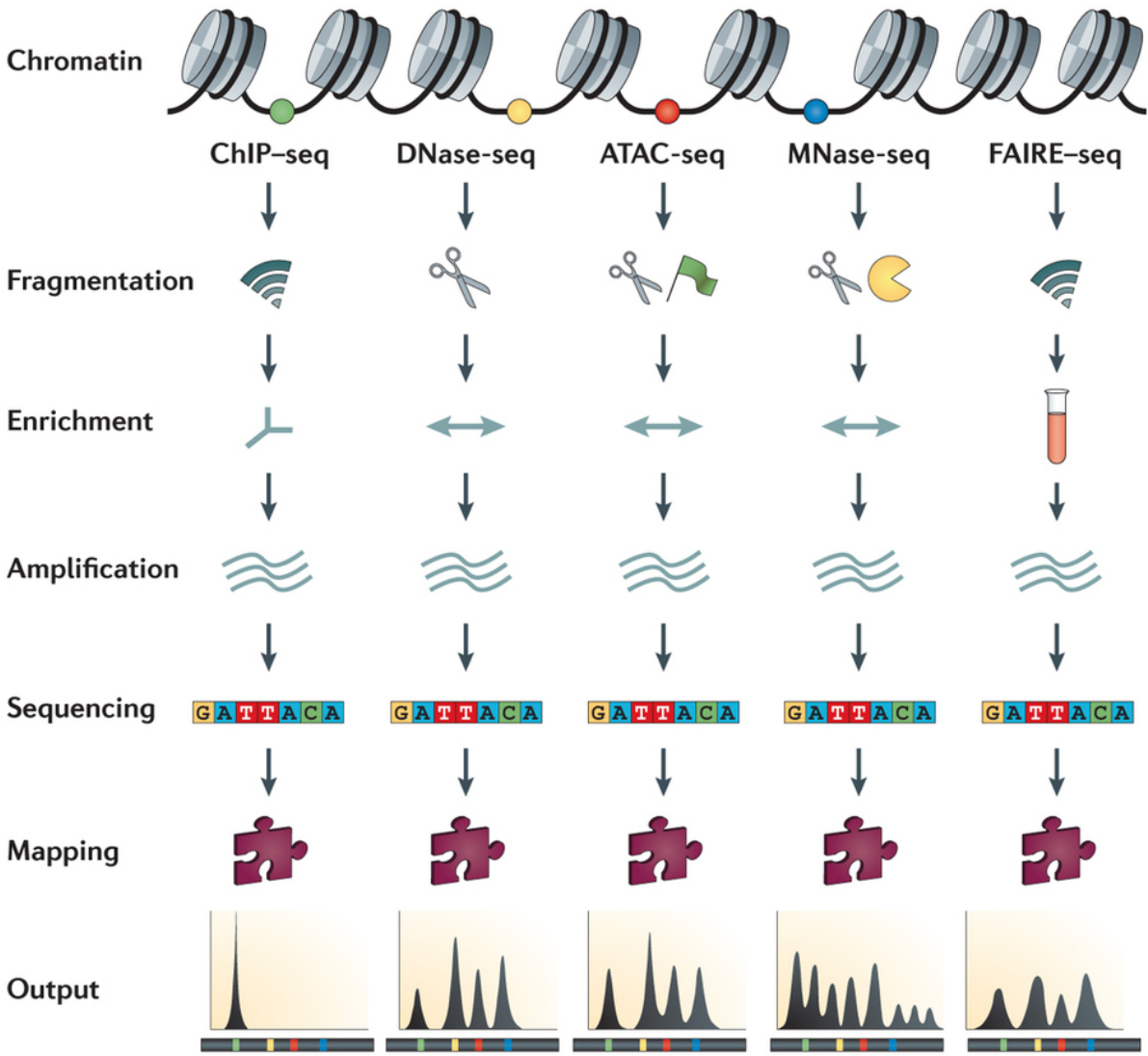
Stockholm, 24 November 2020

Agata Smialowska

NBIS, SciLifeLab, Stockholm University



Functional genomics techniques to probe chromatin states



Accessibility – targeting nucleosome-depleted DNA:

- DNase-seq
- ATAC-seq
- FAIRE-seq (Formaldehyde-Assisted Isolation of Regulatory Elements)

Nucleosome positioning: MNase-seq

Assay for Transposase-Accessible Chromatin (ATAC)-seq

- The method published recently in bulk (Buenrostro et al., 2015) and single cell (Buenrostro et al., 2015)

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UNIT

ATAC-seq: A Method for Assaying Chromatin Accessibility Genome-Wide

Jason D. Buenrostro, Beijing Wu, Howard Y. Chang, William J. Greenleaf



First published: 05 January 2015

<https://doi.org/10.1002/0471142727.mb2129s109>

Citations: 696

Published: 17 June 2015

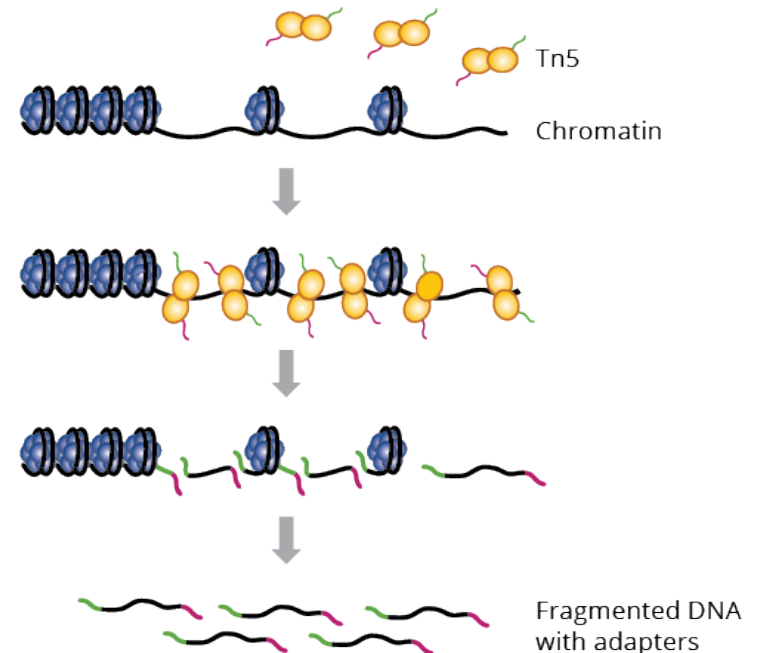
Single-cell chromatin accessibility reveals principles of regulatory variation

Jason D. Buenrostro, Beijing Wu, Ulrike M. Litzénburger, Dave Ruff, Michael L. Gonzales, Michael P. Snyder, Howard Y. Chang  & William J. Greenleaf 

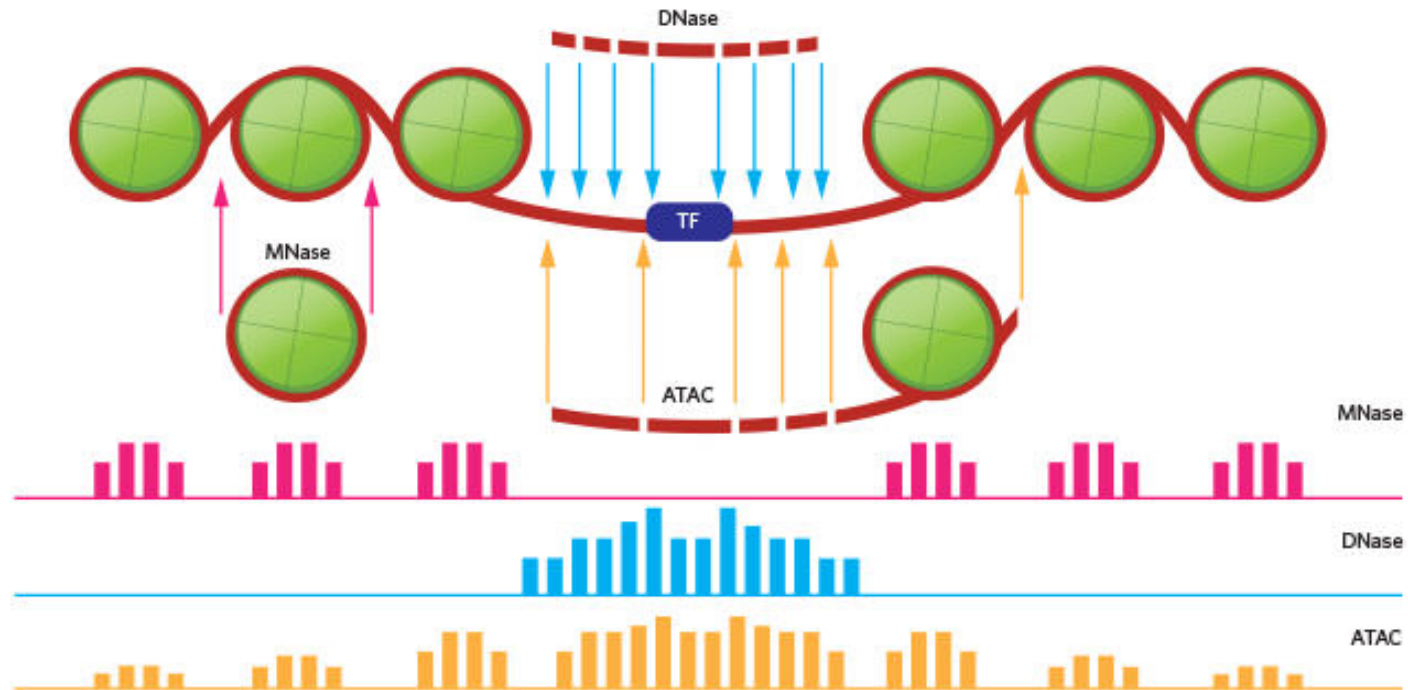
Nature 523, 486–490(2015) | [Cite this article](#)

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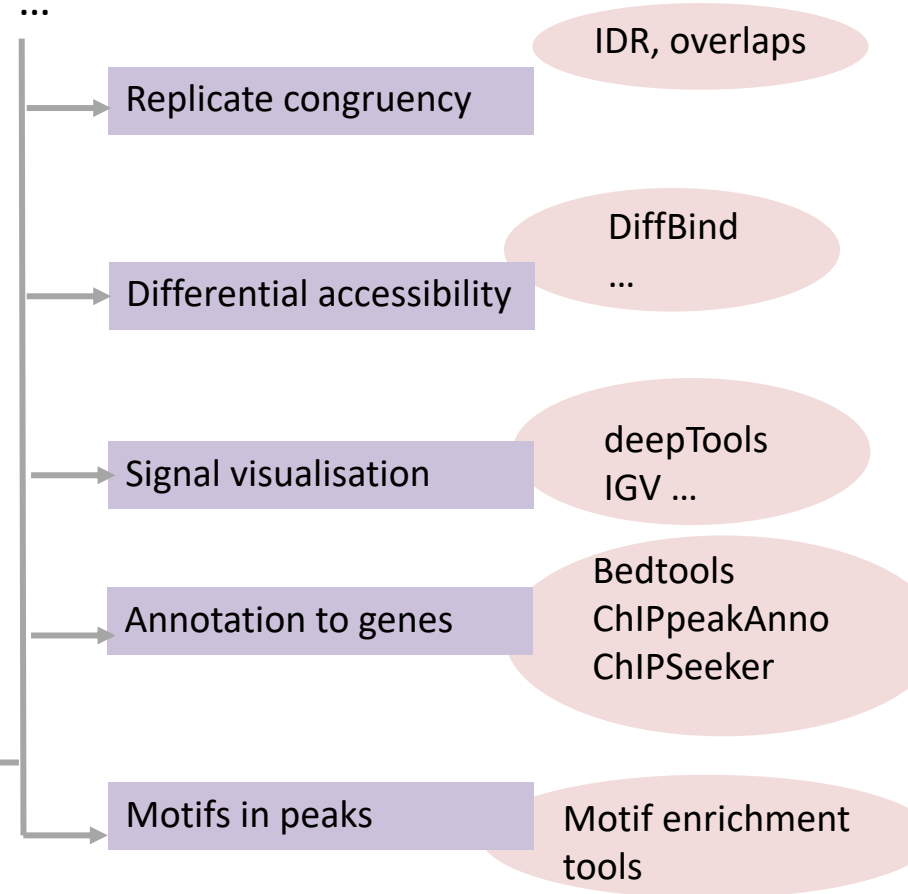
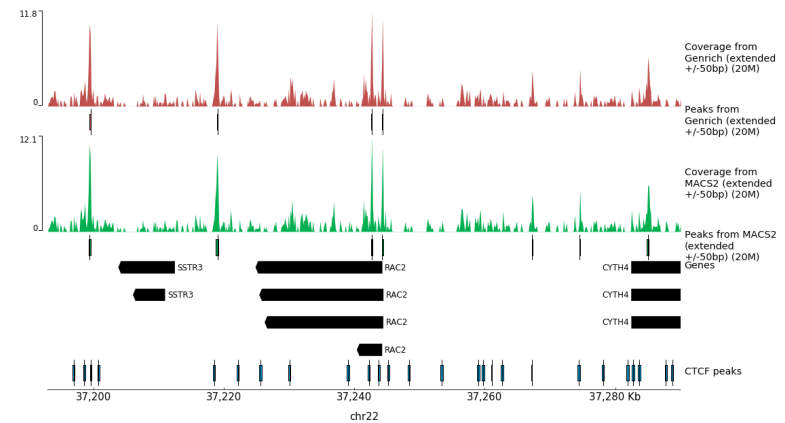
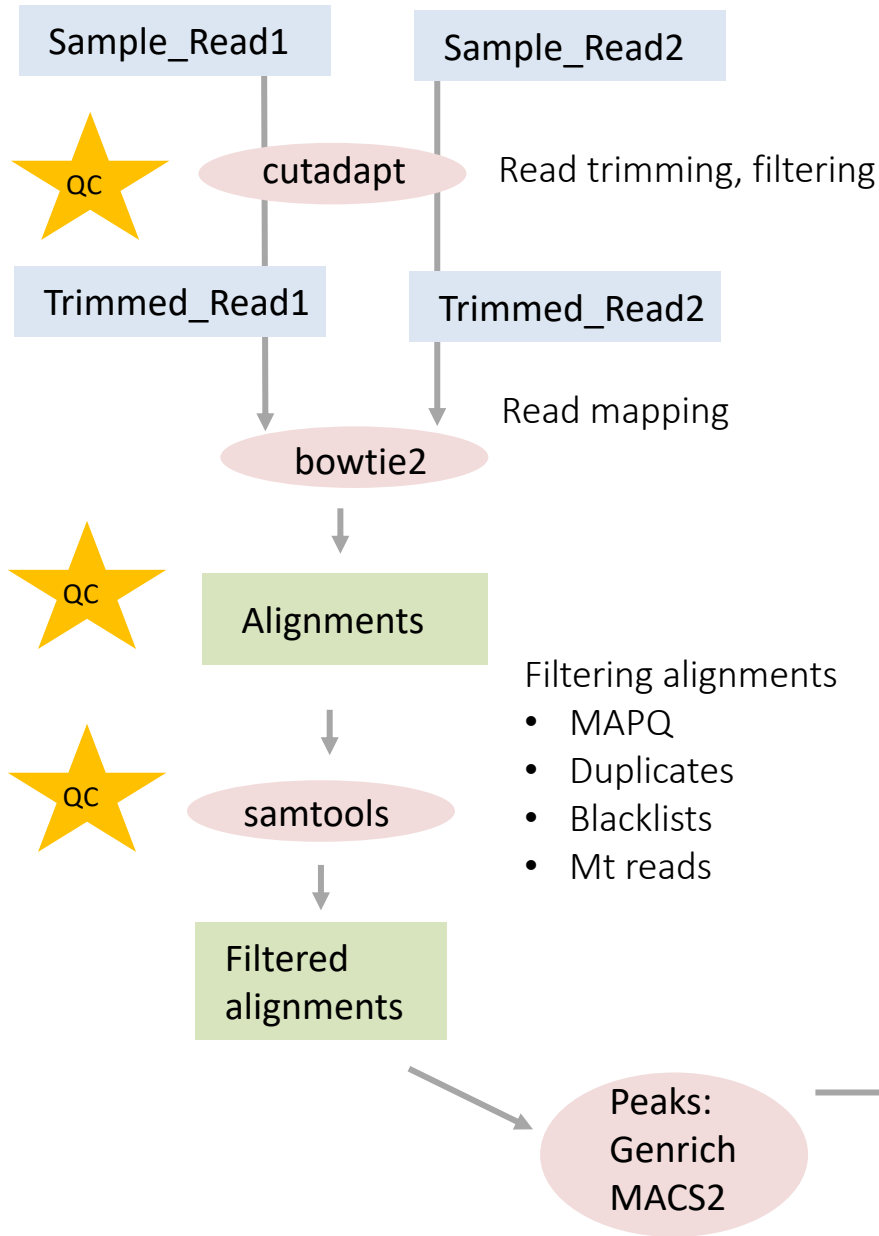
- It probes access to chromatin by using Tn5 transposase to insert sequencing adapters into DNA which allows simultaneous fragmentation of chromatin and integration of those adapters into open chromatin regions
- Significantly fewer cells needed (~ 50,000 cells for ATAC-Seq compared to millions of cells for the other methods (DNase-Seq or FAIRE-Seq))
- Two step process, one day of work



Functional genomics techniques to probe chromatin states

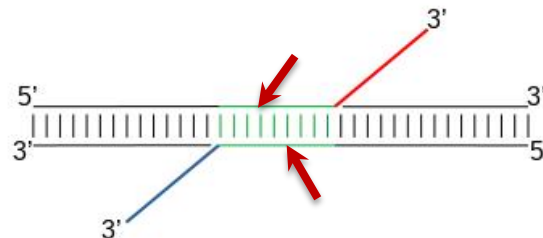


Analysis workflow



Special considerations for ATAC-seq data analysis

- Paired end (PE) sequencing is recommended
- QC: fragment length distribution – mononucleosome peak should be evident
- QC: fraction of mt reads – it can be high (up to 40%) – calculate sequencing depth accordingly
- For current data quality standards, refer to ENCODE; currently 25 million non-duplicate, non-mitochondrial aligned read pairs (i.e. 50M PE reads); non-redundant fraction >0.9; fraction of reads in called peak regions (FRiP) >0.3; TSS enrichment observed
- Peak calling
 - Genrich – peak caller dedicated to ATAC-seq data (has an ATAC-seq mode); PE data only
 - MACS2 – can be used BUT some adjustments are required to center fragments on the Tn5 insertion sites



Resources

R/Bioconductor workflows

- <https://seandavi.github.io/AtacSeqWorkshop/articles/Workflow.html>
- https://rockefelleruniversity.github.io/RU_ATAC_Workshop.html

Galaxy workflows

- <https://training.galaxyproject.org/training-material/>

Bioconductor packages

- ATACseqQC
- esATAC
- ALPS

