

MAESTRO: Model-based AnalysEs of Single-cell Transcriptome and Regulome

Ming (Tommy) Tang

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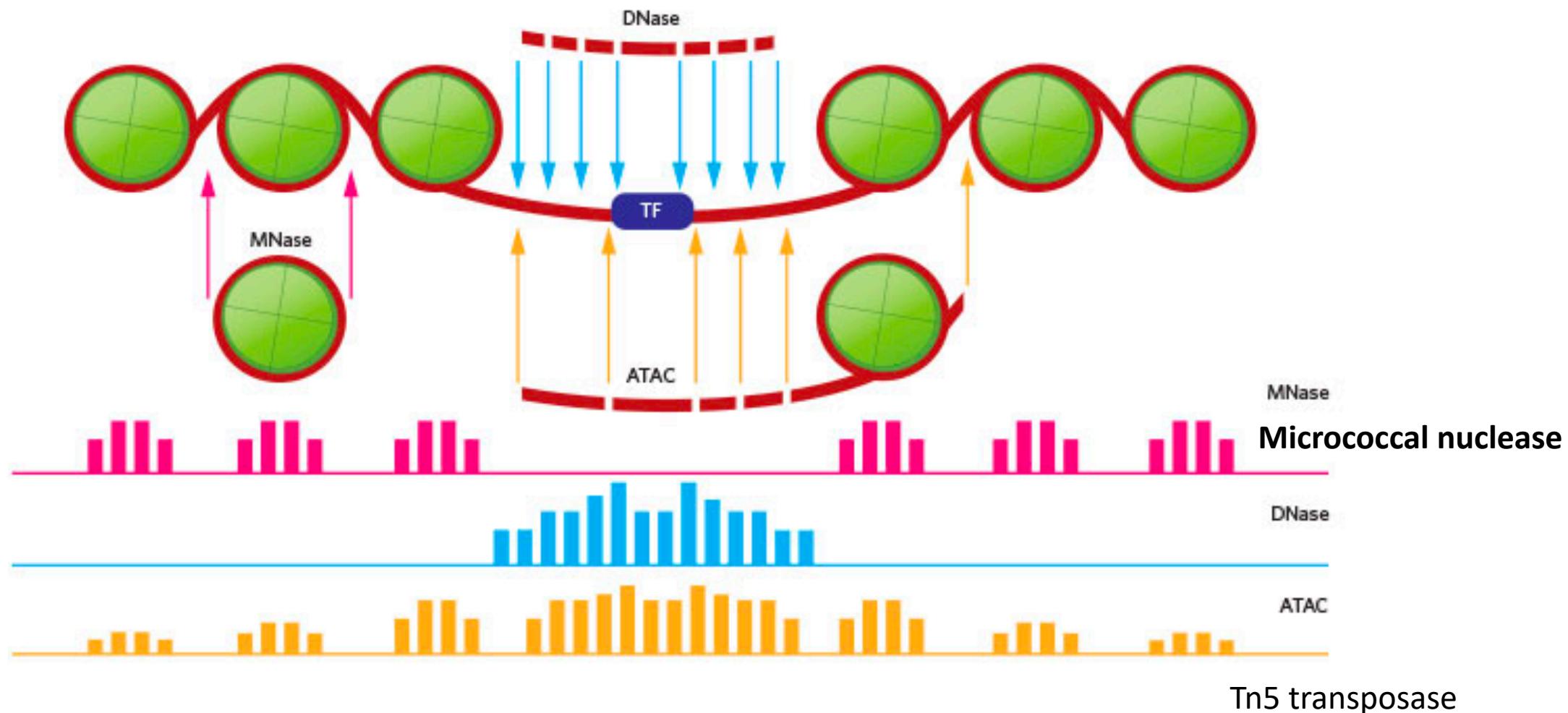
X Shirley Liu group

Senior scientist at Dana-Farber Cancer Institute

<https://divingintogeneticsandgenomics.rbind.io/>



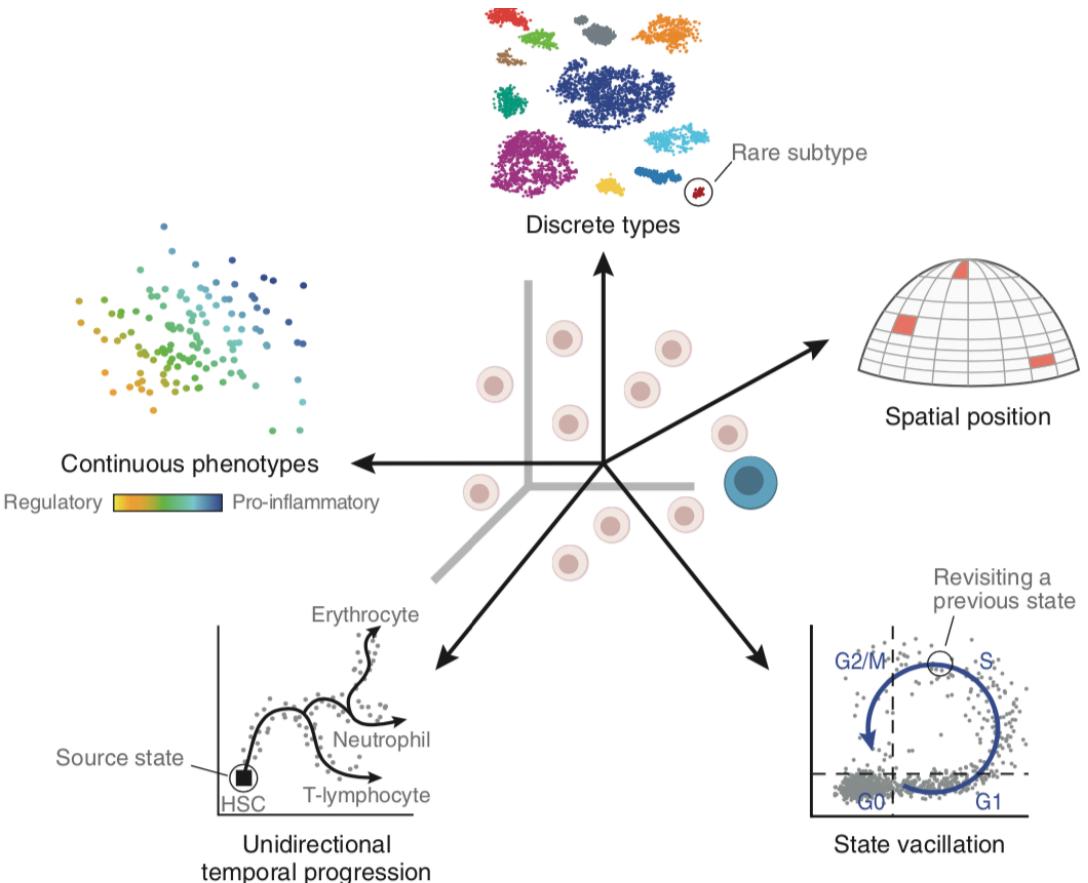
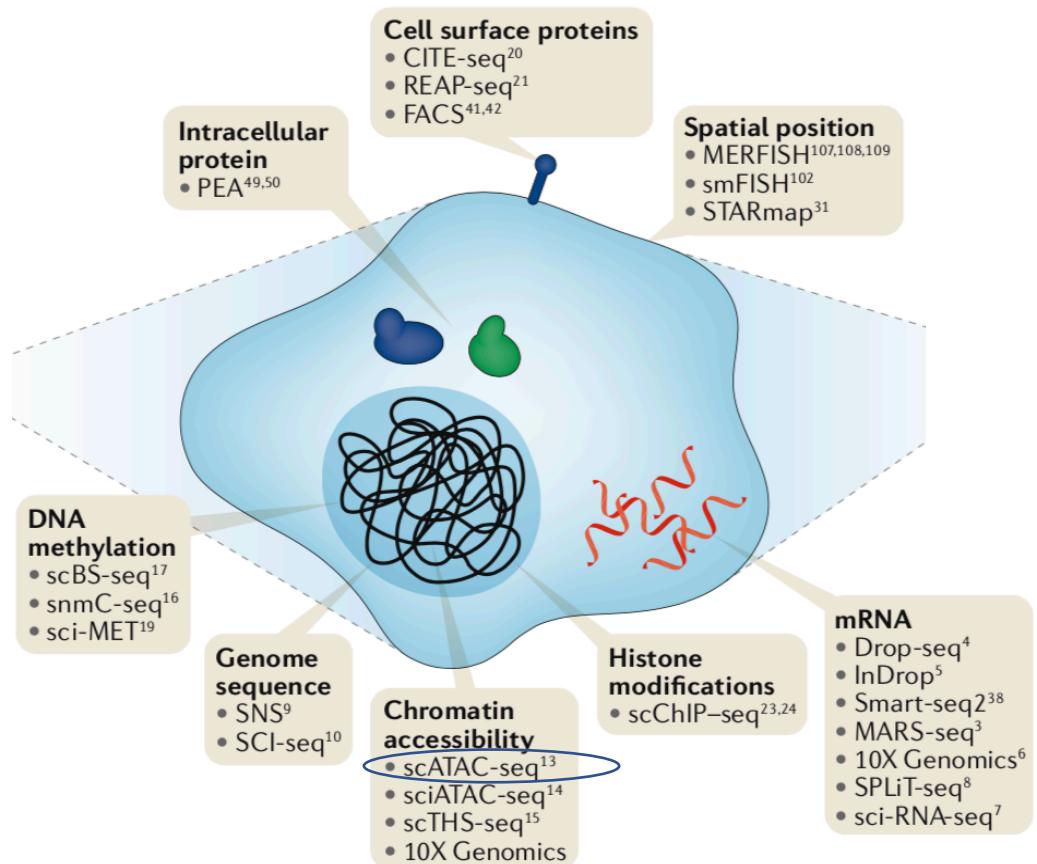
Assays to investigate chromatin accessibility



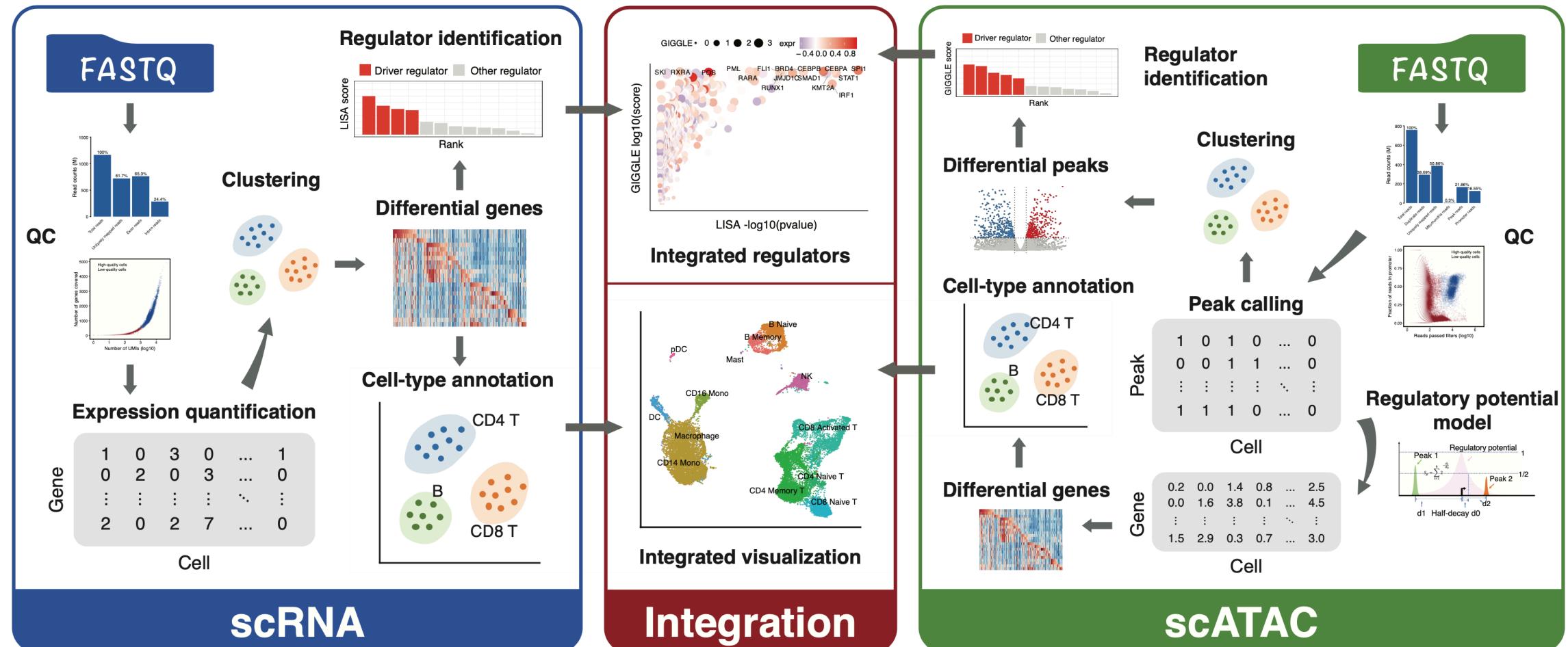
CHIPs: bulk ATAC-seq processing pipeline in CIDC



Analyzing single-cell omics data give insights to biological functions

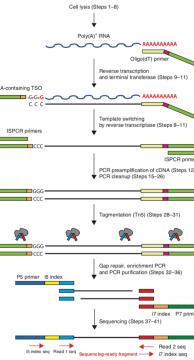


MAESTRO, an integrative analysis workflow based on Snakemake for scRNA-seq and scATAC-seq

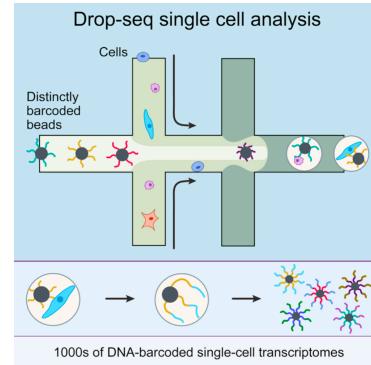


MAESTRO supports data from multiple scRNA-seq and scATAC-seq protocols

scRNA-seq

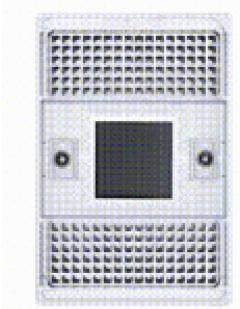


Smart-seq2
Picelli et al., 2014

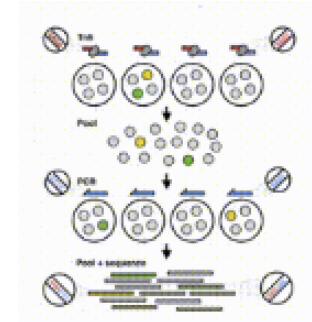


Drop-seq/indrop
Macosko et al., 2015

scATAC-seq



Fluidigm C1
Buenrostro et al., 2015



sci-ATAC-seq/dsci-ATAC-seq
Buenrostro et al., 2015, 2019



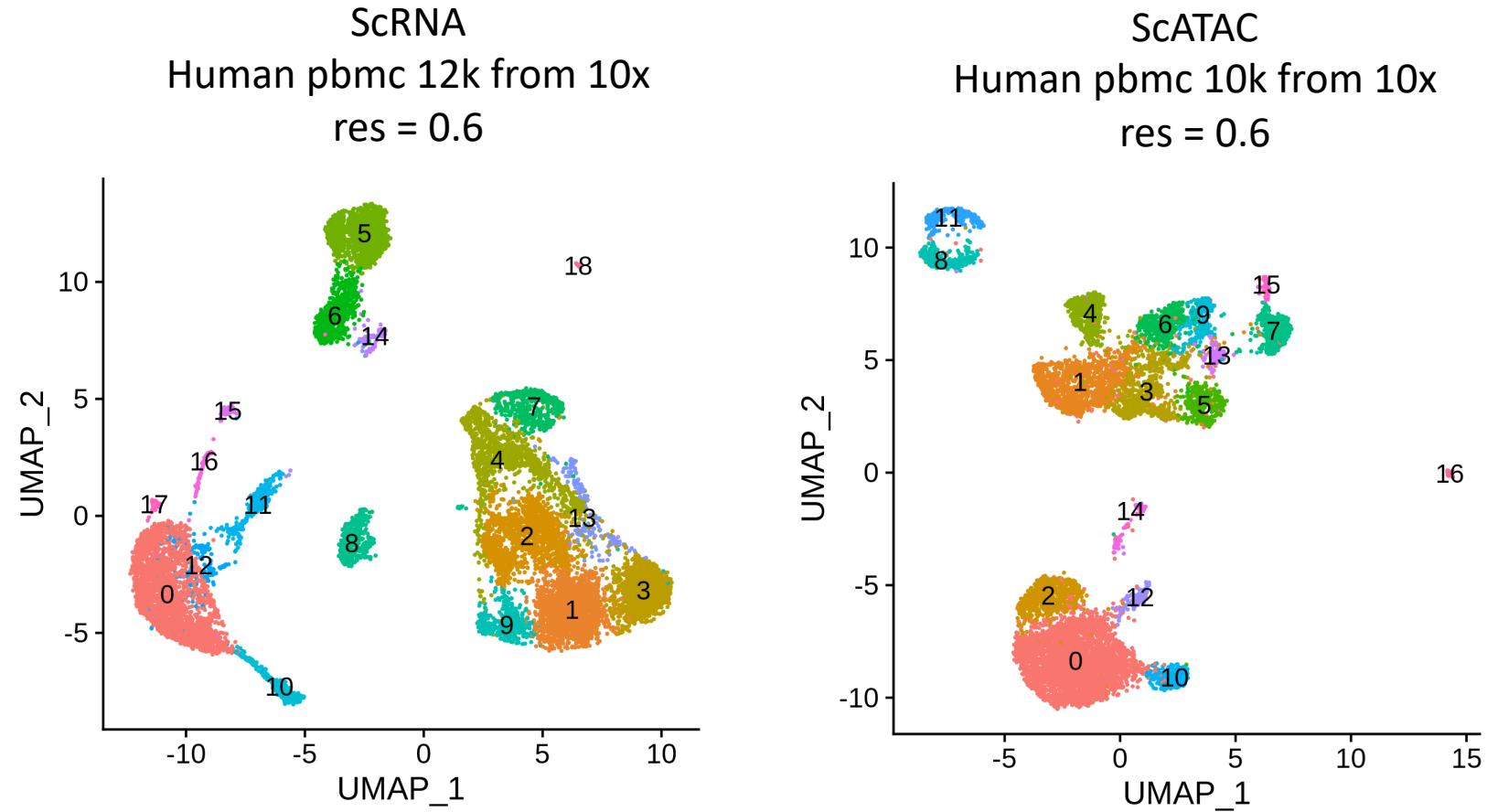
10x genomics
2016



10x genomics
2018

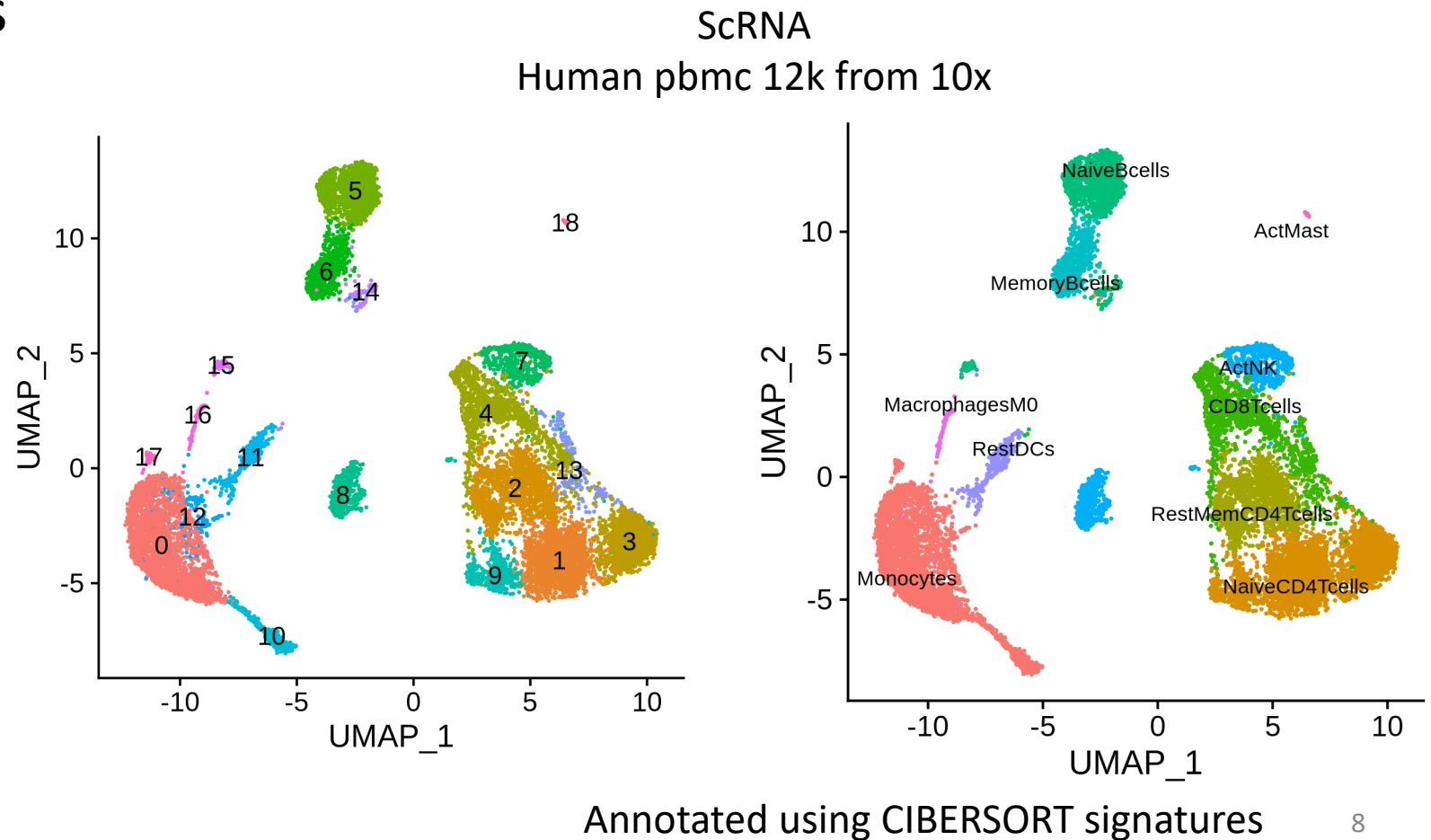
MAESTRO uses the graph-based clustering for scRNA-seq and scATAC-seq

- Dimension reduction
 - ScRNA: PCA
 - ScATAC: Latent semantic index (LSI)
- Build KNN graphs
- Louvain algorithm to detect communities and identify clusters
- Umap visualization



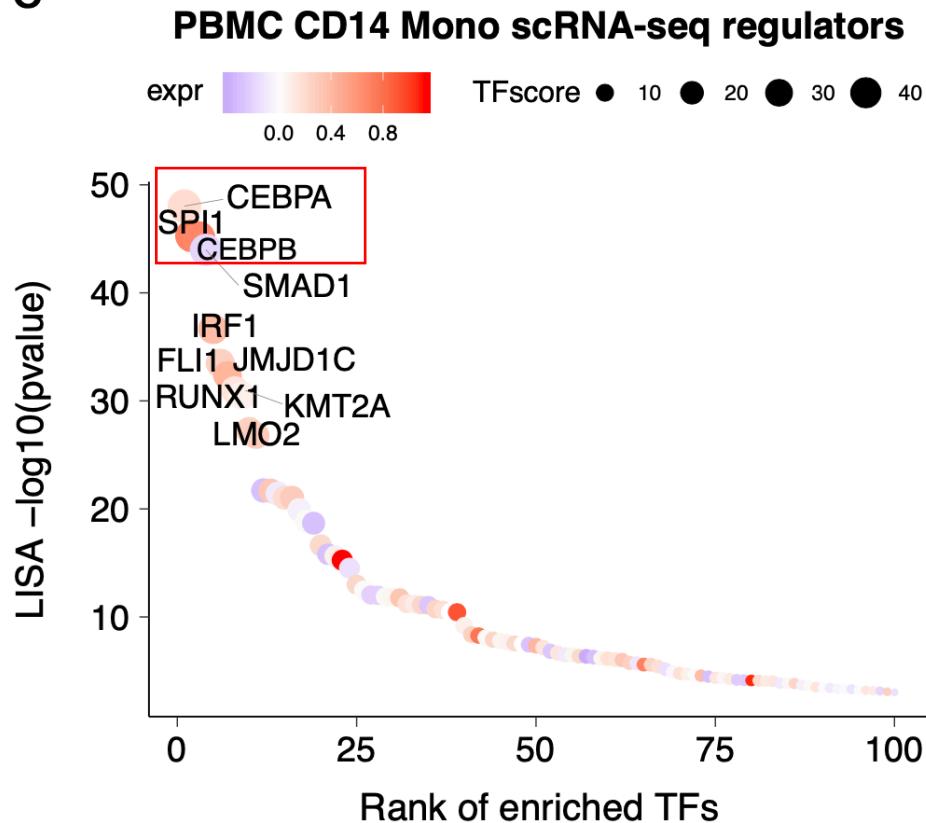
MAESTRO carries out differential expression/accessibility analysis and supports automatic cell type annotation based on gene signatures

- Differential gene analysis
 - Wilcoxon rank sum test
 - DESeq2
 - MAST
- Celltype annotation
 - Gene signature based celltype annotation
 - Logfc based celltype scoring
 - Support user defined gene signatures



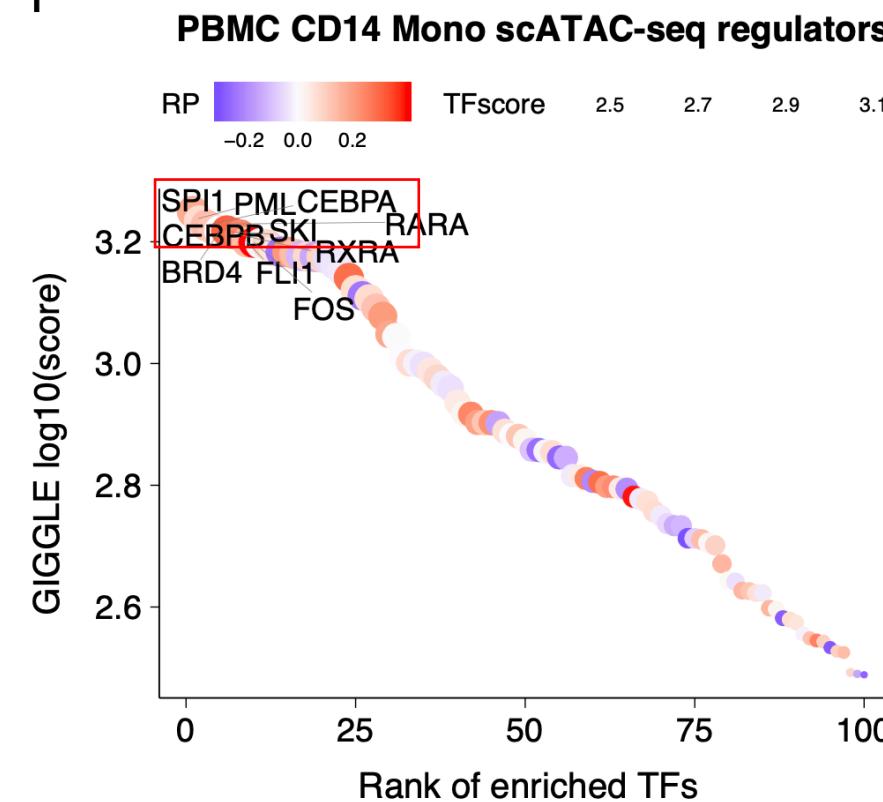
MAESTRO can identify important transcription regulators for both scRNA-seq and scATAC-seq

e



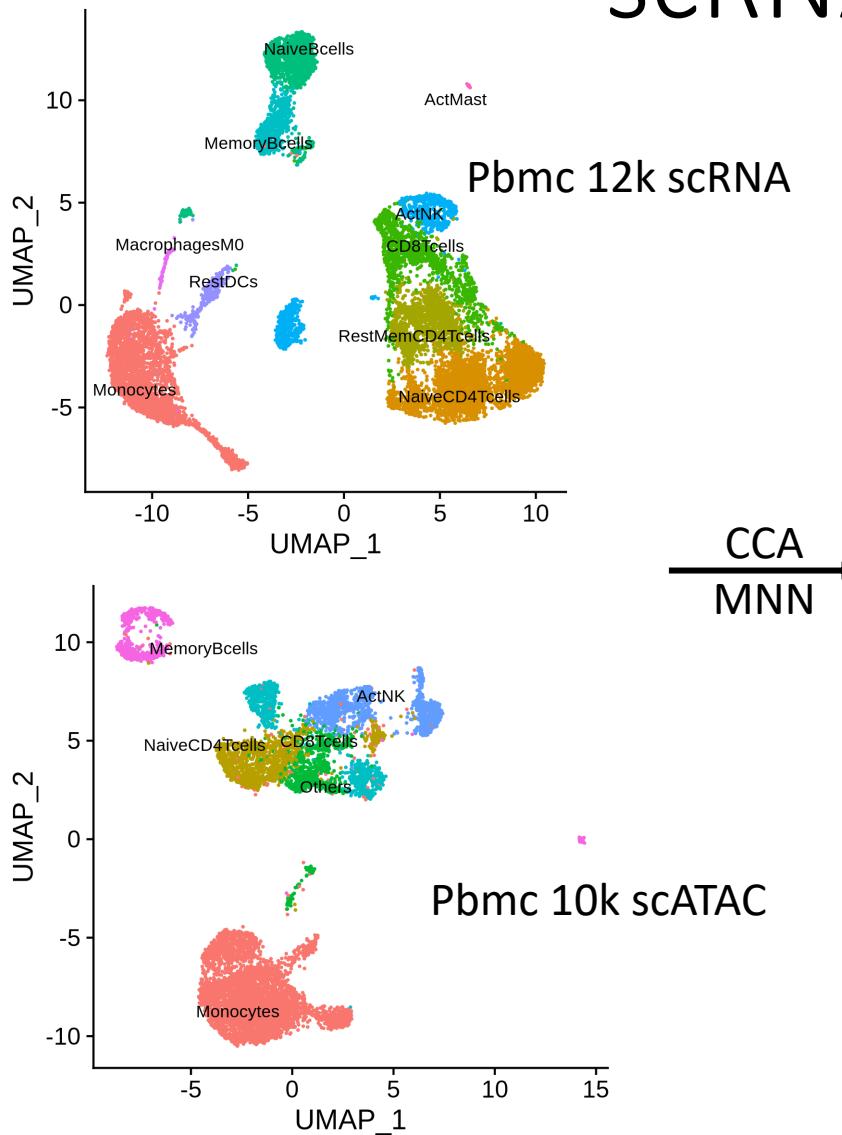
Based on up-regulated genes in each cluster

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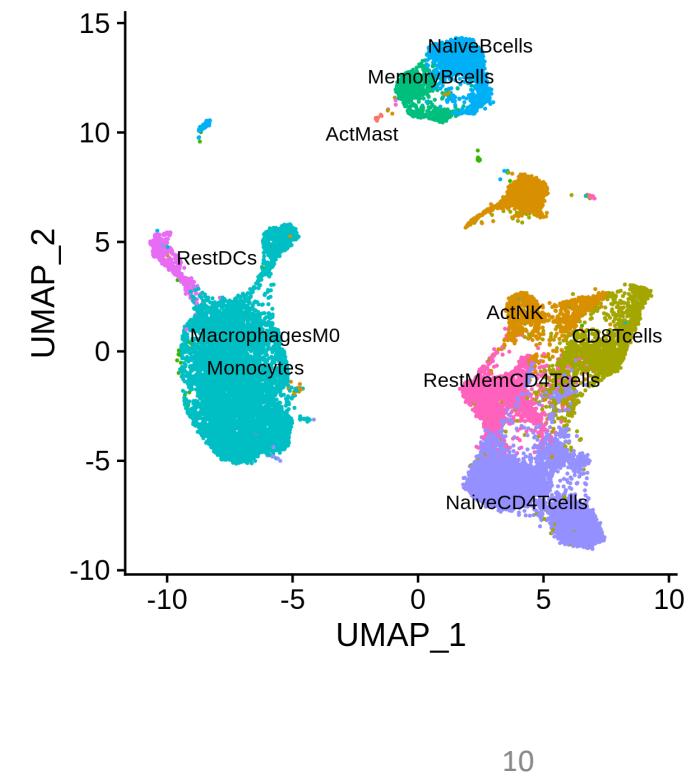
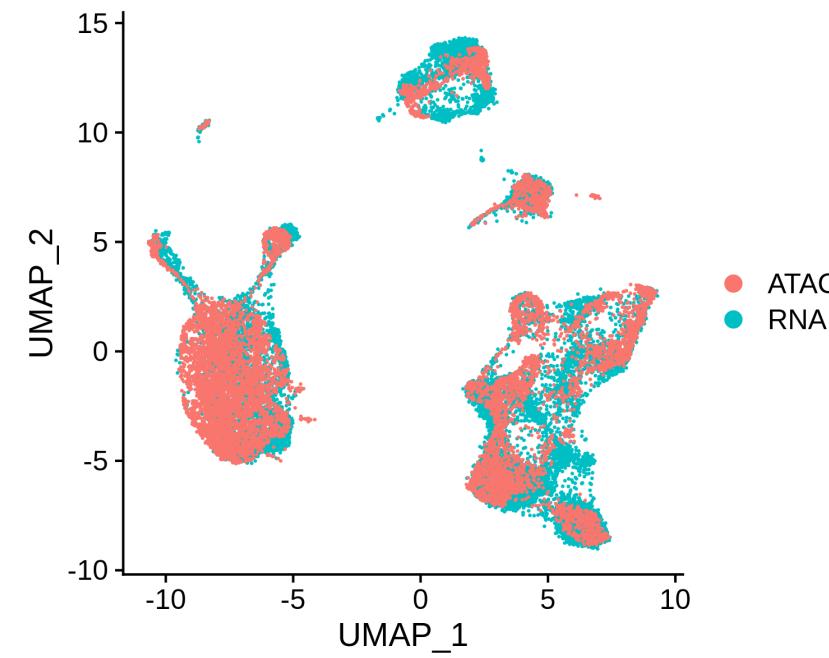


Based on positive peaks in each cluster

MAESTRO provides integrated clustering of scRNA-seq and scATAC-seq



ScRNA and scATAC integrated
Human pbmc from 10x



Summary

- MAESTRO, an integrative scRNA-seq and scATAC-seq analysis workflow supporting multiple experimental protocols.
- MAESTRO provides utilities from the basic alignment, QC to high level functional analysis
- MAESTRO uses the best practice for single cell clustering
- MAESTRO enables transcription regulation analysis for both scRNA-seq and scATAC-seq data based on CistromeDB.
- ScATAC-seq regulatory potential (RP) score outperforms other existing methods in predicting gene expression level and integration with scRNA-seq data.

The future of MAESTRO

- keep adding new features and fixing bugs.
- faster processing scATAC-seq data.
- multi-sample scRNA-seq and scATAC-seq processing.

<https://github.com/liulab-dfci/MAESTRO>

Full solution of MAESTRO can be installed using Conda

Acknowledgements

CIDC Bioinformatics team:

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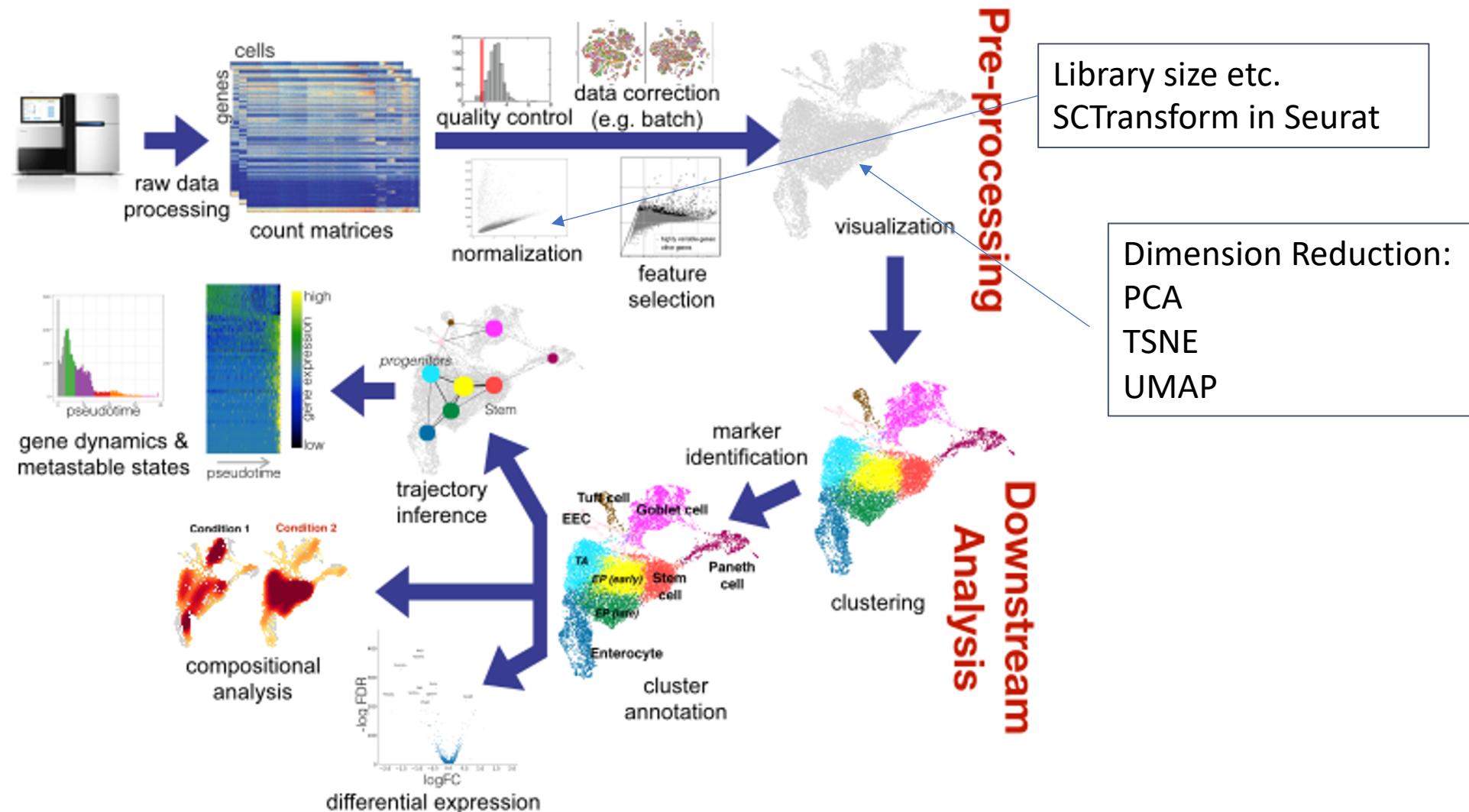
Dana-Farber
Cancer Institute

Breakout topic: scATAC-seq

Discussion leader: Ming (Tommy) Tang

- What are the pros and cons of this technology?
- What is the fit for CIMAC trials?
- Relative level of optimization/standardization/reliability?
- Any other comments/considerations?

Workflow of a typical* scRNA-seq analysis

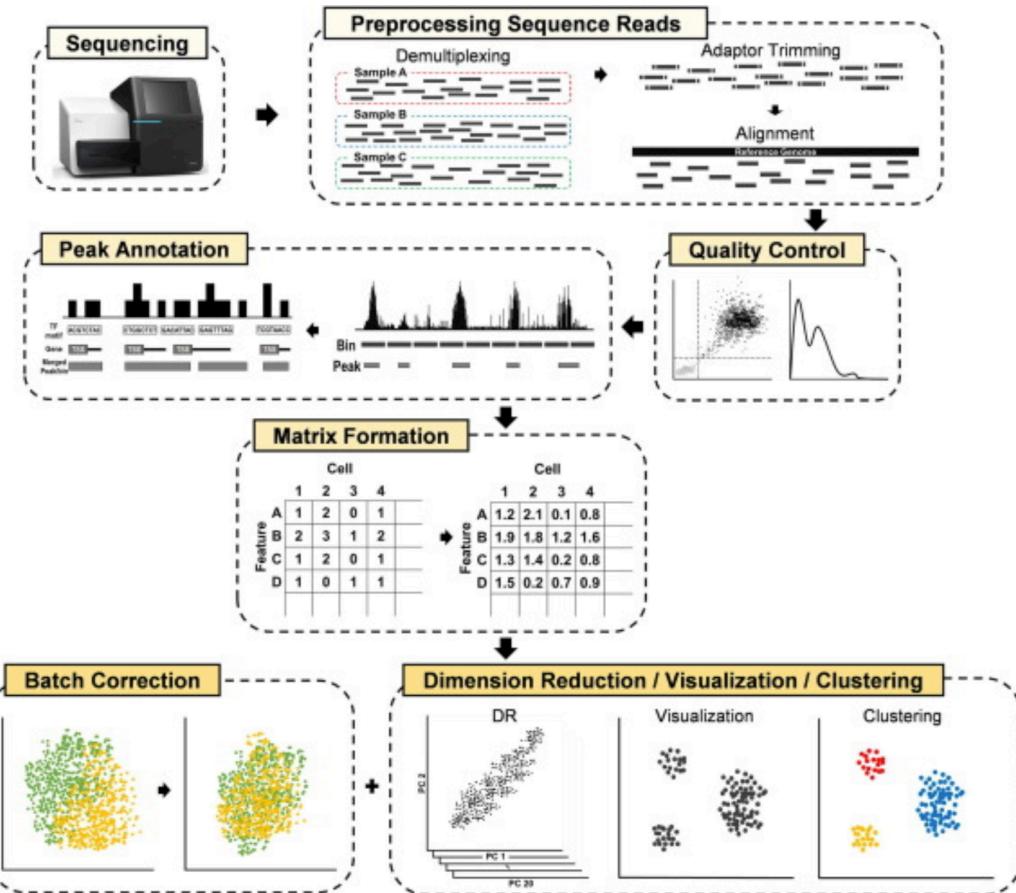


Credit to Peter Hickey

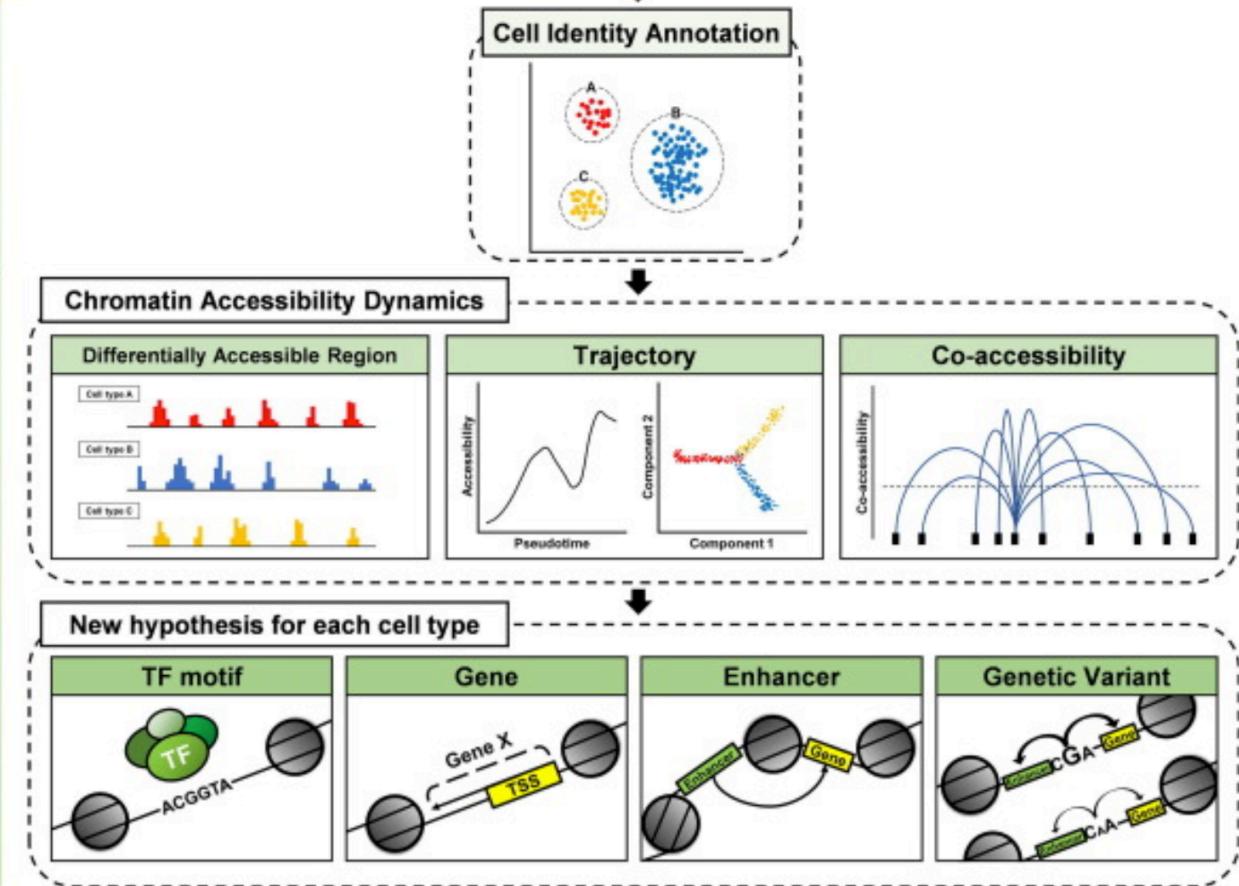
[Luecken, M. D. & Theis, F. J. Current best practices in single-cell RNA-seq analysis: a tutorial. *Mol. Syst. Biol.* 15, \(2019\).](#)

scATAC-seq processing steps

Pre-processing



Downstream Analysis

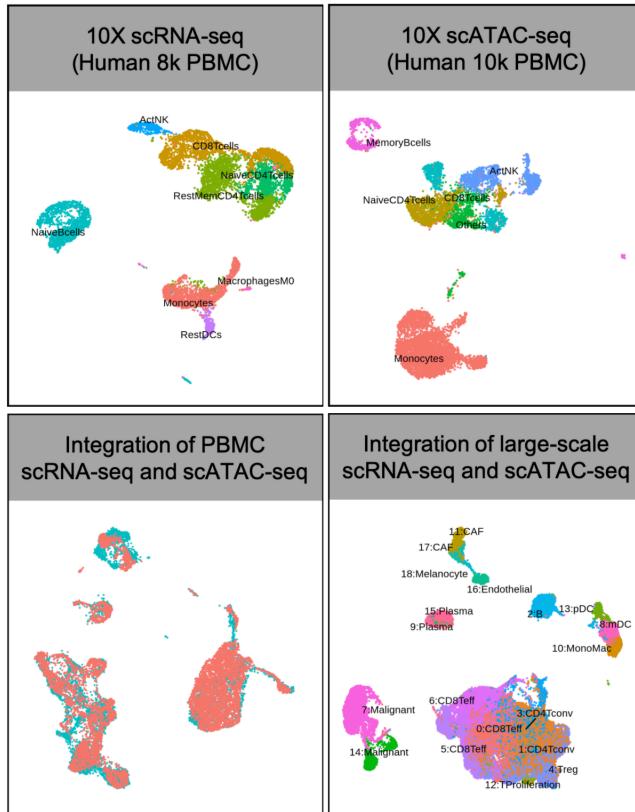


MAESTRO is easy to install and generates an html report for various QC metrics

<https://github.com/liulab-dfci/MAESTRO>

Full solution of MAESTRO can be installed using Conda.

Documents @



Html output example @

