Scalable, multimodal profiling of chromatin accessibility, protein levels and mitochondrial genotypes in single cells

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a

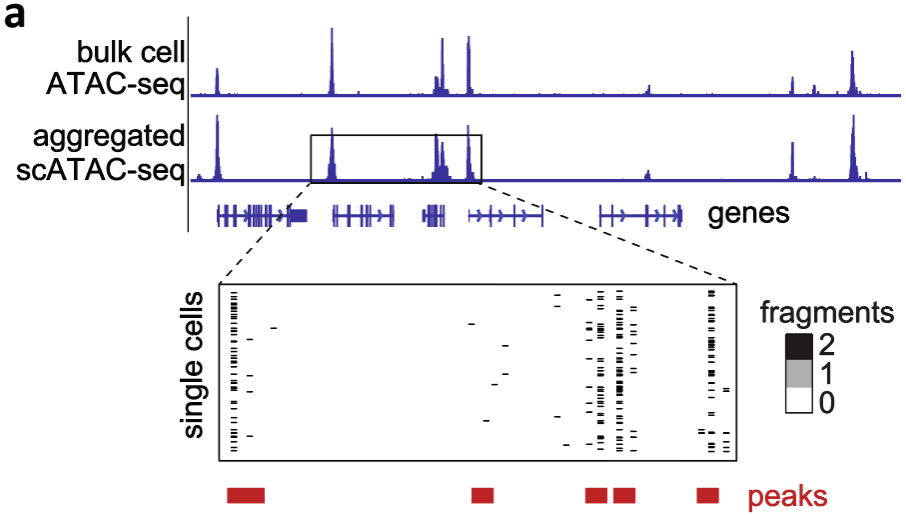
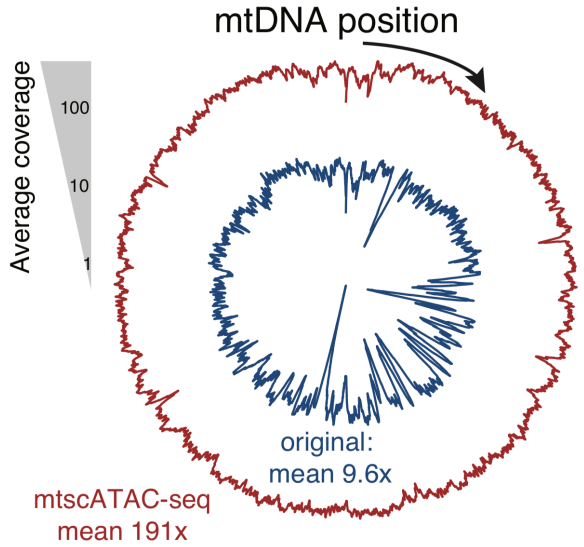


Figure adapted from Chen et *al*. *Genome Biology* 2019

b



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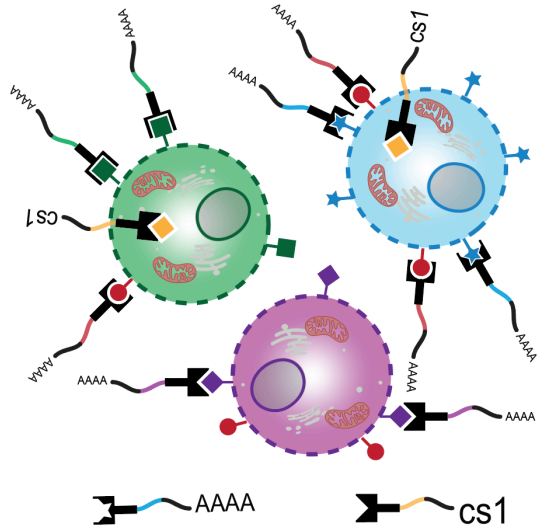


Single cell Assay for Transposase-Accessible Chromatin by sequencing (**scATAC-seq**)

→ Gene regulatory elements

→ Transcription factor activity

Mitochondrial **mtscATAC-seq**

→ Whole mtDNA genome sequencing

→ Germline and somatic mutation detection for clonal tracing and mitochondrial disease studies

ATAC-seq with Surface Antigen Profiling by sequencing (**ASAP-seq**)

→ Co-detection of surface and intracellular proteins

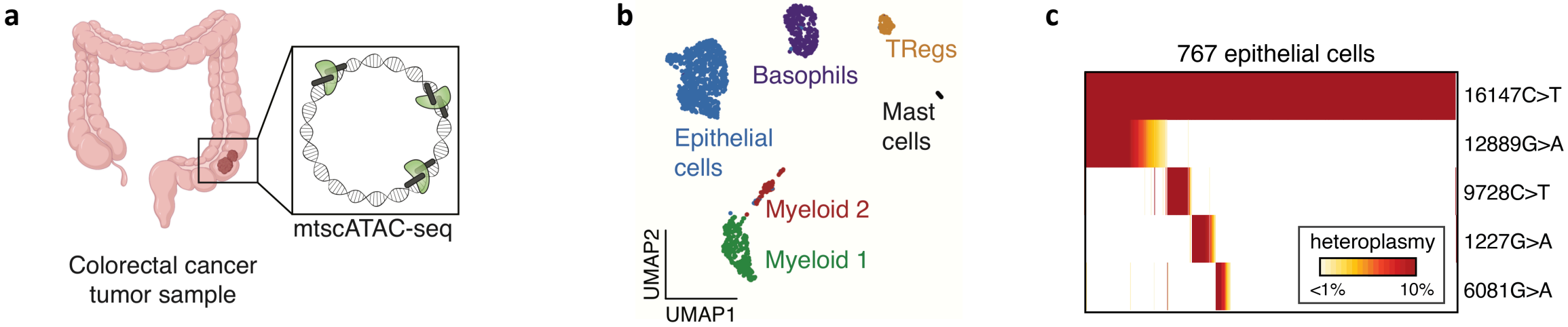
Lareau*, Ludwig* et *al*. *Nature Biotechnology* 2020
Walker*, Lareau*, Ludwig* et *al*. *New England Journal of Medicine* 2020

https://cite-seq.com/asapseq/
Mimitou*, Lareau*, Chen* et *al*. *BioRxiv*

mtscATAC-seq → mitochondrial and nuclear mutations resolve clonal structures in human colorectal cancer

Somatic mitochondrial mutations and copy number variants detected from mtscATAC-seq data

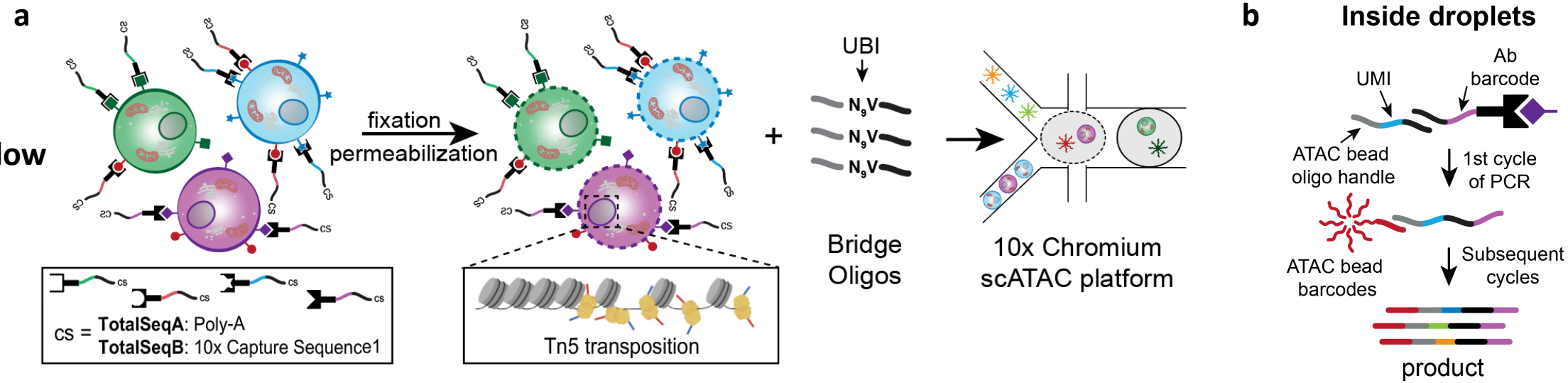
- Combined detection of different types of somatic variants presents a powerful means to better resolve subclonal structures and associated clonal phenotypes and evolutionary processes in malignancies



Lareau*, Ludwig* *et al*. *Nature Biotechnology* 2020

ASAP-seq enables co-detection of surface markers and intracellular proteins

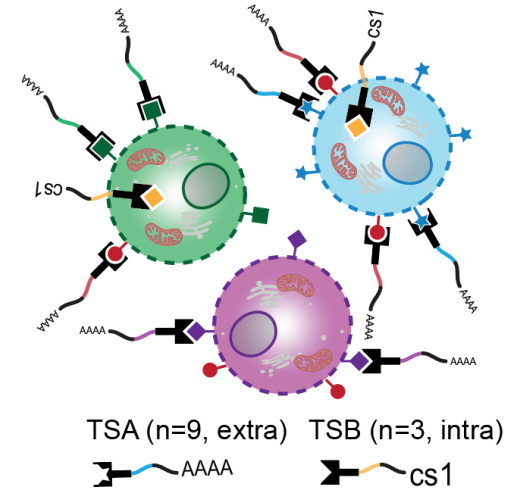
Workflow

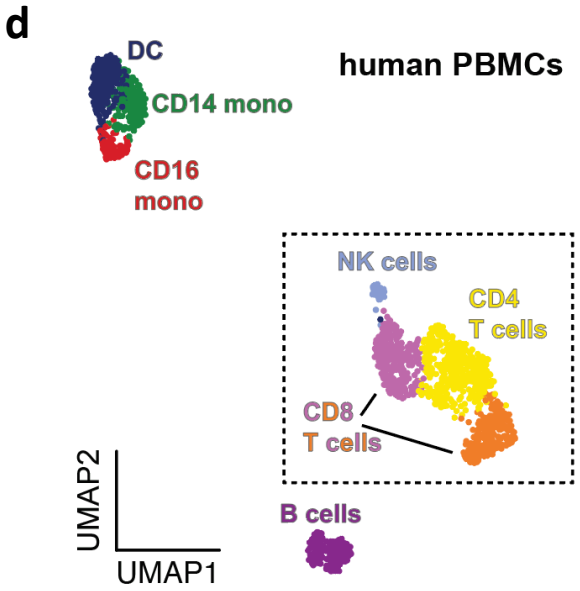


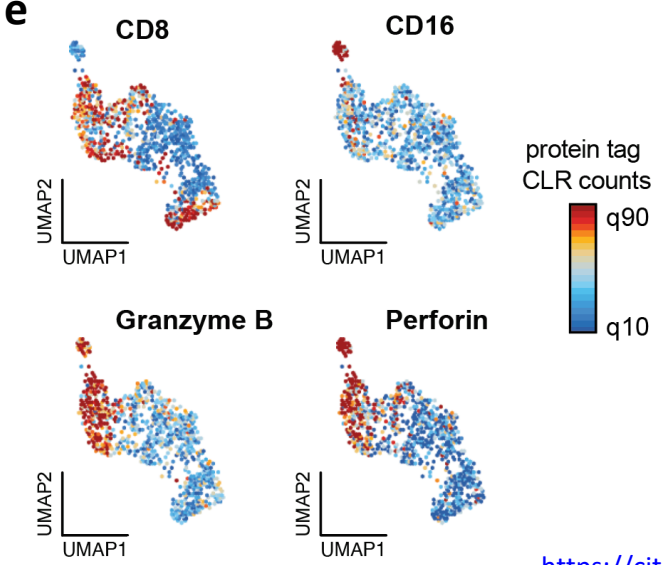
Intracellular staining

- Use of different oligo handles

- Specific staining of Granzyme B and Perforin in NK and cytotoxic T cells



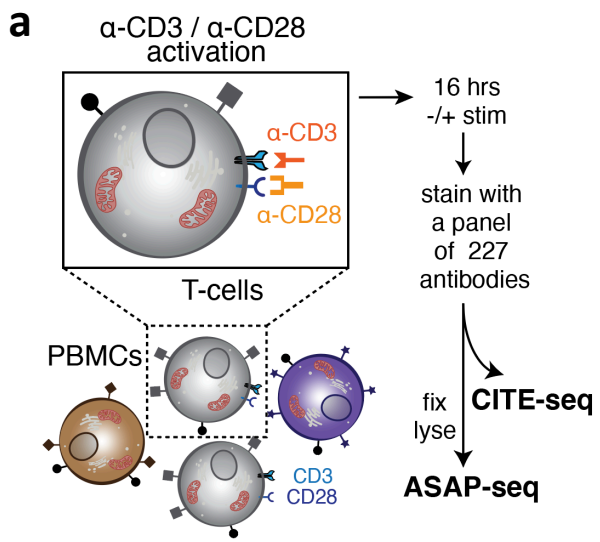


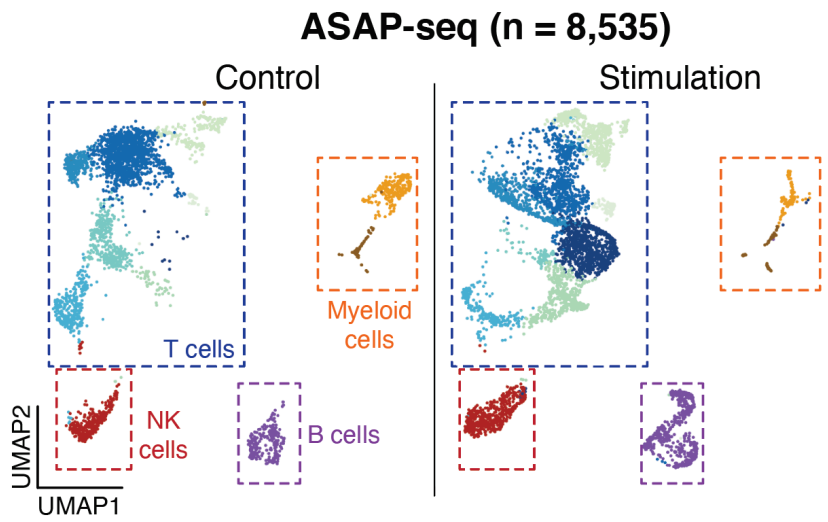


https://cite-seq.com/asapseq/

Mimitou*, Lareau*, Chen* *et al. BioRxiv*

Combined CITE- & ASAP-seq of anti-CD3/CD28 stimulated human PBMCs

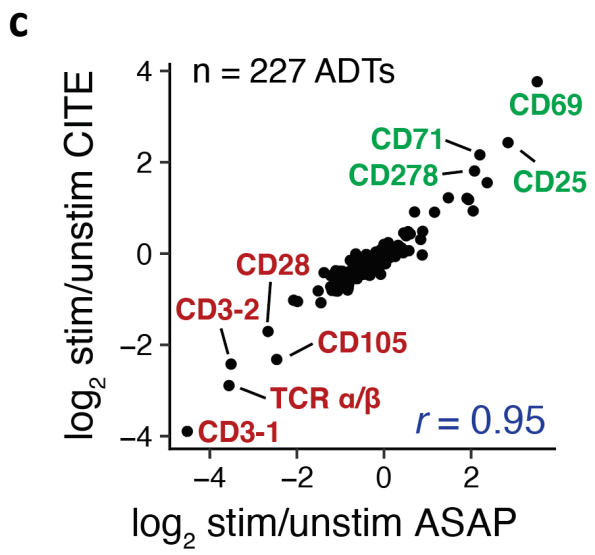


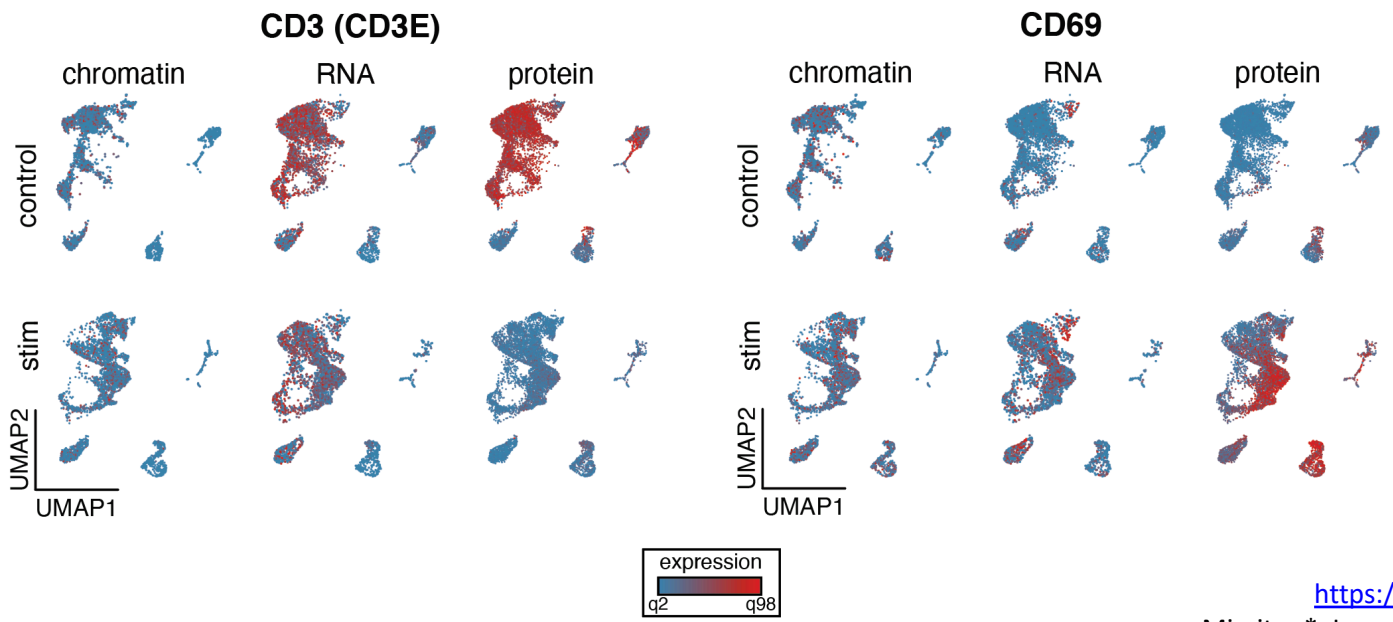


a,b) Anti-CD3/CD28 stimulation of peripheral blood mononuclear cells leads to pronounced changes in T cell states

c) Changes in surface marker expression are concordant in CITE-seq and ASAP-seq workflows

d) Surface marker proteins and changes in levels may be more sensitively detected than RNA and accessible chromatin levels and can also be decoupled.





PBMCs = peripheral blood mononuclear cells

https://cite-seq.com/asapseq/

Mimitou*, Lareau*, Chen* *et al. BioRxiv*