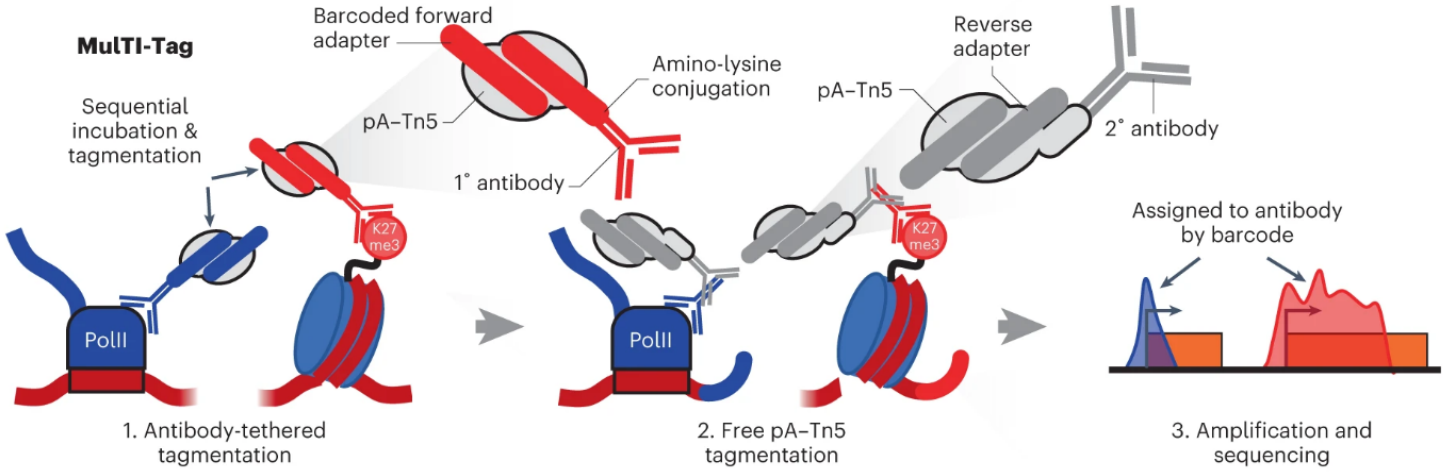
Single Cell Transcriptomics

Newsletter December 2022

Paper 1

Meers, MP *et al.* [Multifactorial profiling of epigenetic landscapes at single-cell resolution using MulTI-Tag], *Nature Biotechnology*, 2022-10-31

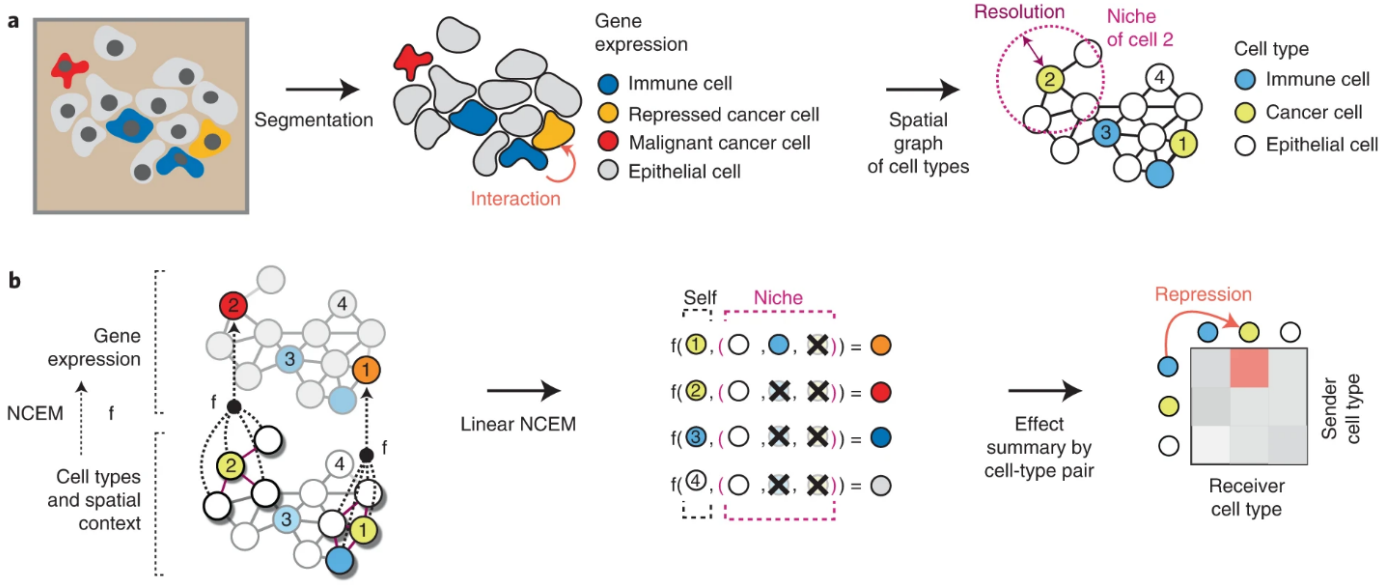
The first paper of the month describes an antibody barcoding approach for profiling multiple chromatin features simultaneously in single cells through Multiple Target Identification by Tagmentation (MulTI-Tag). The idea behind MulTI-Tag resides in the possibility to profile multiple epigenome characteristics at once to derive important information about cell-type-specific epigenome patterns at specific loci. As such, MulTI-Tag allows for physical association of a chromatin protein-targeting antibody with an identifying adapter barcode added during tagmentation to deconvolute epigenome targets directly in sequencing. Meers *et al*. demonstrate detection of three histone modifications in the same cell: H3K27me3, H3K4me1/2 and H3K36me3 and conclude how multifactorial epigenetic profiling holds promise for comprehensively characterizing cell-specific gene regulatory landscapes in development and disease.



Paper 2

Fischer, DS *et al.* [Modeling intercellular communication in tissues using spatial graphs of cells](), *Nature Biotechnology*, 2022-10-27

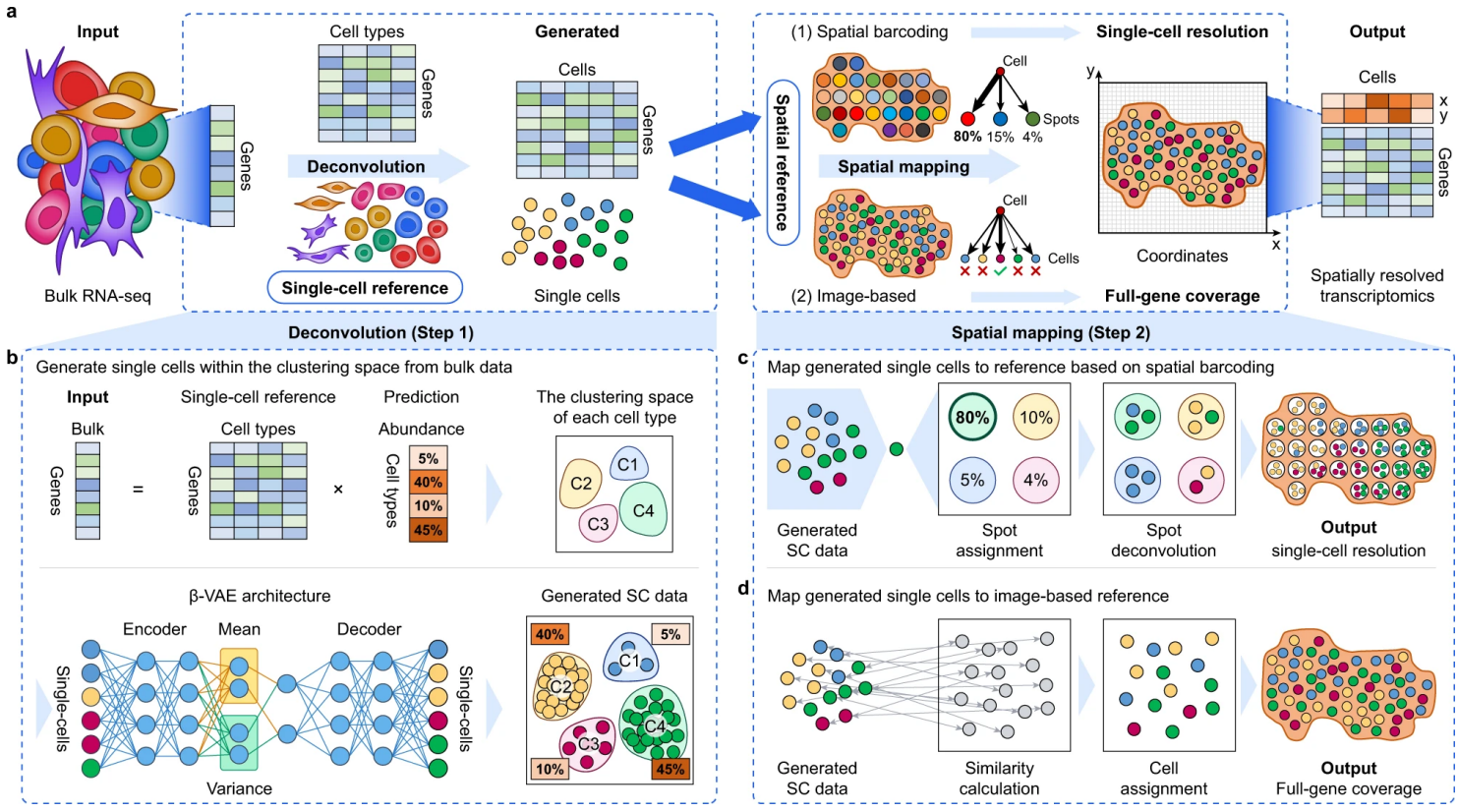
The second paper is a brief communication from Theis lab regarding how models of intercellular communication in tissues are based on molecular profiles of dissociated cells, and that these models are limited to receptor–ligand signaling and ignore spatial proximity in situ. Fischer *et al*. presents node-centric expression modeling, a method based on graph neural networks that estimates the effects of niche composition on gene expression in an unbiased manner from spatial molecular profiling data. The authors were able to recover signatures of molecular processes known to underlie cell communication. Furthermore, they demonstrated how their method, using spatial graph representations, can model niches and may be exploited for unsupervised analysis of tissue structures.



Paper 3

Liao, J *et al.* De novo analysis of bulk RNA-seq data at spatially resolved single-cell resolution, *Nature Communications*, 2022-10-30

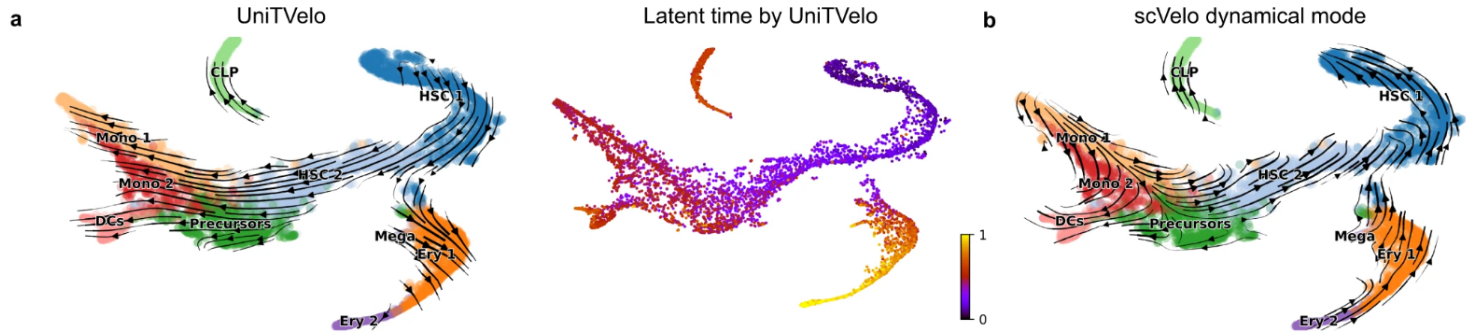
The next paper concerns the exploitation of widely available bulk RNA-seq to disclose the spatial and cellular heterogeneity of bulk RNA-seq data using existing single-cell and spatial transcriptomics references. This is performed using a deep learning framework-based spatial deconvolution algorithm named Bulk2Space. Using bulk transcriptomics to validate Bulk2Space unveiled the spatial variance of immune cells in different tumor regions, the molecular and spatial heterogeneity of tissues during inflammation-induced tumorigenesis, and spatial patterns of novel genes in different cell types. Additionally, Liao *et al.* were able to reconstruct the hierarchical structure of the mouse isocortex, and further annotate cell types that were not identified by original methods in the mouse hypothalamus.



Paper 4

Gao, M *et al.* UniTVelo: temporally unified RNA velocity reinforces single-cell trajectory inference, *Nature Communications*, 2022-11-03

The last paper deals with RNA velocity. As pointed out by Gao *et al*., the existing RNA velocity methods are often found to return erroneous results, partly due to model violation or lack of temporal regularization. The authors present UniTVelo, a statistical framework of RNA velocity that models the dynamics of spliced and unspliced RNAs via flexible transcription activities. Uniquely, it also supports the inference of a unified latent time across the transcriptome. Using existing datasets, the authors demonstrate that UniTVelo returns the expected trajectory in different biological systems, including hematopoietic differentiation and those even with weak kinetics or complex branches. As an example shown below, **a** UniTVelo correctly identifies trajectories going from HSC to differentiated immune cells as opposed to an existing method, scVelo **b**. Additionally, the current implementation of UniTVelo benefits from GPU acceleration. Hence, UniTVelo may prove an important tool for RNA velocity and trajectory calculations.



Next Single Cell Seminar

Date: 16th December 2022, Panum Faculty Club, room 16.6.16

9:00 – 10:00

PhD student Katarina Dragicevic, Khodosevich lab

Hiding in plain sight: uncovering diseased interneuron subtypes in a 15q.13.3+/- schizophrenia mouse model

10:00 – 11:00

PhD student Petar Todorov, Pers lab

How to use your single-cell data to select spatial probes

If you would like to announce anything single cell related, e.g. job announcement, event, your published paper, technology development etc., please contact us.

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