DANISH SINGLE-CELL NETWORK NEWSLETTER

APRIL - 2023

THIS MONTH'S HIGHLIGHTS:

Microfluidics-free single-cell genomics with templated emulsification

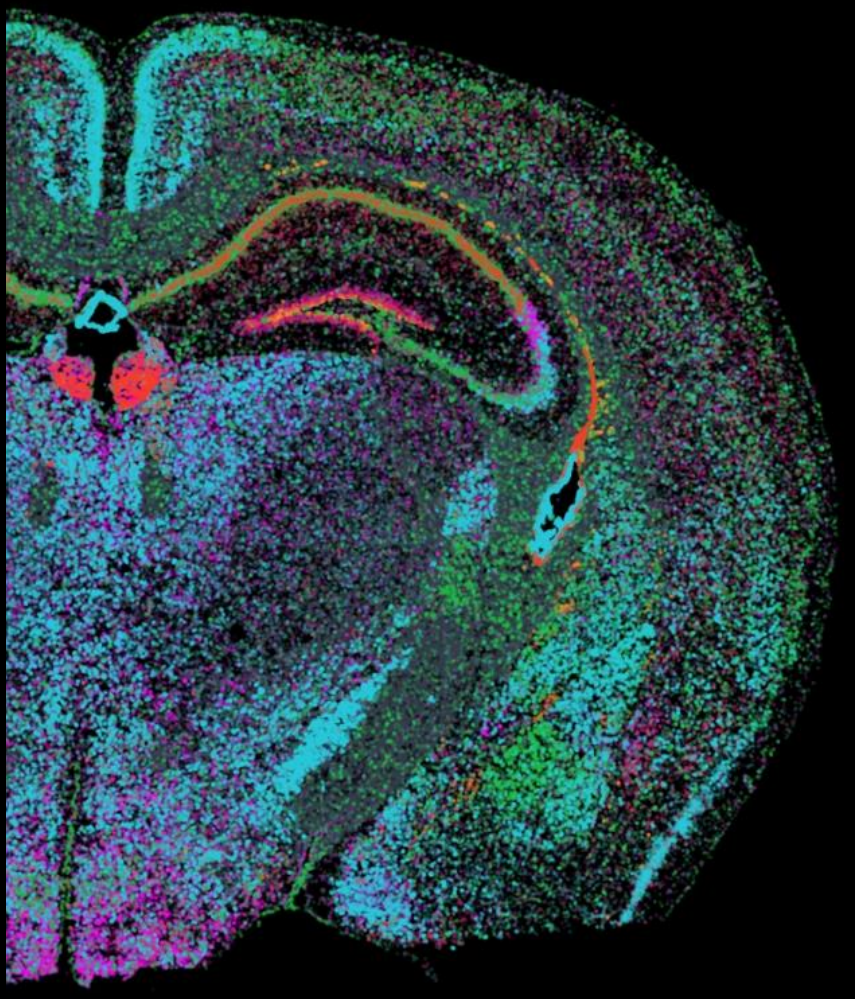
Clark, I. *et al.*

SEACells infers transcriptional and epigenomic cellular states from single-cell genomics data

Persad, S., Choo, ZN., Dien, C. *et al.*

A molecularly defined and spatially resolved cell atlas of the whole mouse brain

Zhang M. *et al.*



COVER IMAGE
Credit: Vizgen Inc.
Title: The Vizgen MERFISH Mouse Brain Receptor Map (2021)

UNIVERSITY OF COPENHAGEN

UPCOMING EVENT

3rd Danish Single Cell Meeting:
Biotechnology and Application to Biology

https://singlecell.ku.dk/3rd-danish-single-cell-meeting-biotechnology-and-application-to-biology/

!CHANGE OF VENUE!

Time and place: Auditorium 4, Universitetsparken 2, 2100 Copenhagen Ø (dinner & postersession at Mærsk Tower, Blegdamsvej 3B, 2200 København N)

!CHANGE OF VENUE!

Deadline for registration:
Extended to 5th of April, remember to register

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Microfluidics-free single-cell genomics with templated emulsification

Clark, I. *et al. Nature Biotechnology (2023),* https://doi.org/10.1038/s41587-023-01685-z

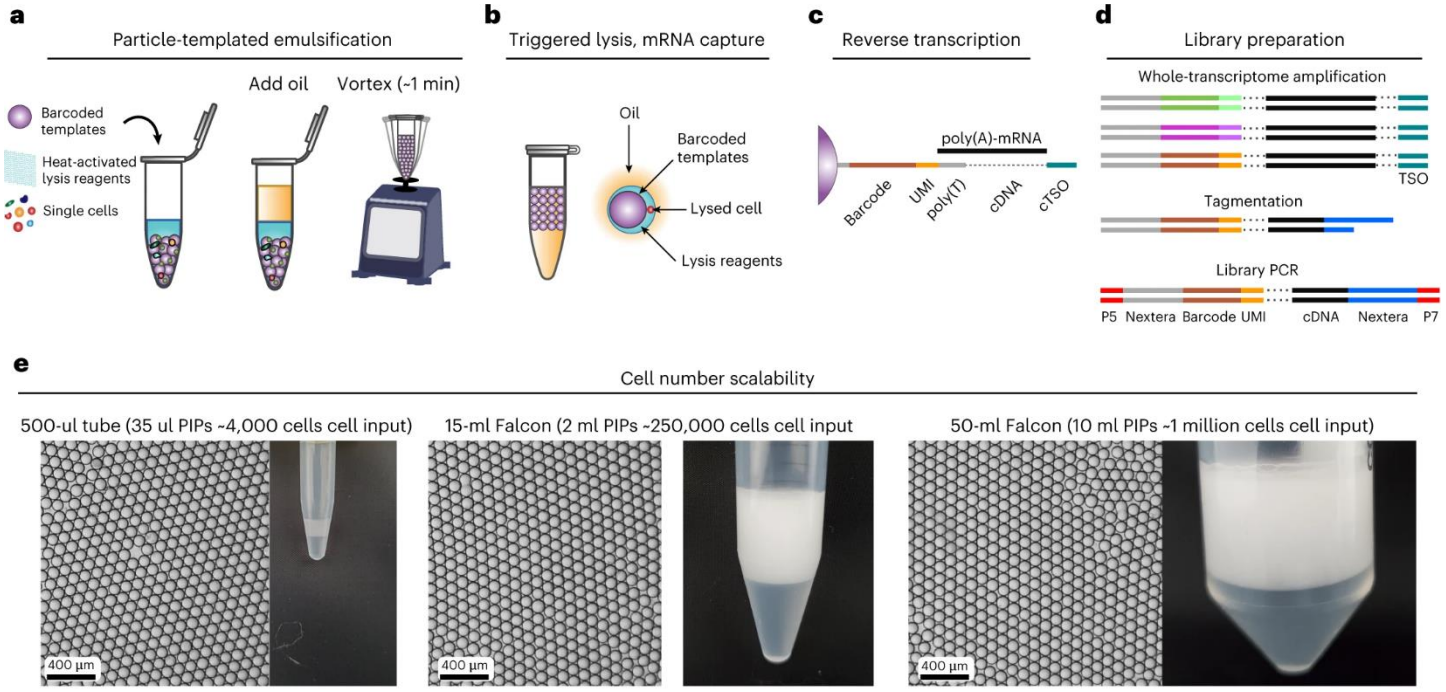

Figure 1. Overview of PIP-seq. The method enables high quality microfluidics free single-cell transcriptomic workflows with high scalability.

In the first newsletter-paper of the month the authors present a new single-cell RNA sequencing (scRNA-seq) method called **PIP-seq** that is simple, rapid, and scalable. PIP-seq uses a **simplified emulsification technique** that produces high-quality data, making it suitable for large-scale and genome-wide Perturb-seq experiments and large cell atlas studies. The authors confirmed the accuracy of PIP-seq by profiling heterogeneous tissue and directly comparing their results to the well established 10x Chromium scRNA-seq platform. The PIP-seq cell-type classification, marker identification, and **gene expression levels were tightly matched with 10x data, but PIP-seq detected fewer genes per cell.**

The authors evalute the method with clinical samples by profiling the relapse of mixed-phenotype acute leukemia (MPAL) after chemotherapy. PIP-seq identified transcriptional heterogeneity beyond that observed by immunophenotype and suggested that therapeutics targeting ribosomal biogenesis and/or protein translation may have therapeutic potential in MPAL.

The power of this method is without question the **microfluidics free approach**, that enables users to process samples with high throughput, without the tidous pipeting numerous other methods require, and abolish the risk of microfluidic malfunction resulting in loss of precious sample. Futher, the scalability allows users to **break through cell loading limits** of many current methods, thus getting higher throughput and unleash the full potential of samples by not having to discard leftover material.

SEACells infers transcriptional and epigenomic cellular states from single-cell genomics data

Persad, S., Choo, ZN., Dien, C. *et al. Nature Biotechnology* (2023), https://doi.org/10.1038/s41587-023-01716-9

Persad *et al.* present in this article **SEACell**, which is a new method for identifying **metacells in single-cell** data that overcomes sparsity and retains the rich heterogeneity of the data. It improves integration across samples and scaling analysis to large cohort-based datasets. SEACells is particularly adept at identifying rare cell states, which often represent critical populations that drive biology or disease. SEACells identifies more compact, better separated, and more evenly distributed metacells than existing methods. **It is the only method currently able to derive cell states from scATAC-seq** data in an accurate and comprehensive manner, greatly empowering gene regulatory inference.

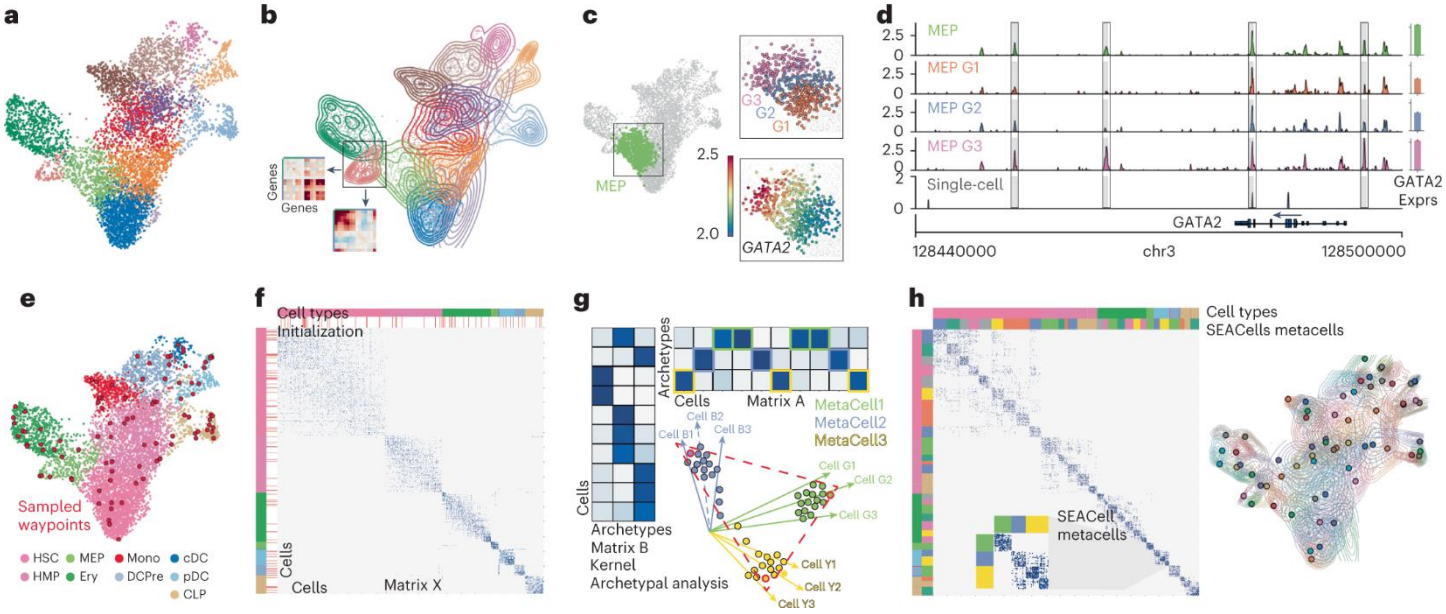

Figure 2. Overview of SEACells. The methods provides a graph-based algorithm that uses kernel archetypal analysis to compute metacells. This enables identifaction of metacells which provide robust and comprehensive characterizations of cell states and these describe chromatin cell states at sufficient resolutions to resolutions that permit the enference of regulatory elelments underlying gene expression.

SEACells metacells can be computed separately for each sample, rendering the integration of additional cohort members resource-efficient. This provides a more robust representation of sample-specific biology, thus serving as better input for data integration. SEACells identified COVID-19-enriched CD4+ T cell states that are removed by typical batch correction and undetected at the single-cell level. SEACells metacells facilitate the distinction of biological signal from batch effect, enabling the discovery of the T cell state continuum. Overall, **SEACells provides a scalable solution for integrating large datasets from cohorts**, improving fundamental ATAC analysis, and enabling more sophisticated regulatory network inference, promising wide utility in single-cell chromatin profiling data.

A molecularly defined and spatially resolved cell atlas of the whole mouse brain

Zhang M. *et al. bioRxiv* (2023), https://doi.org/10.1101/2023.03.06.531348

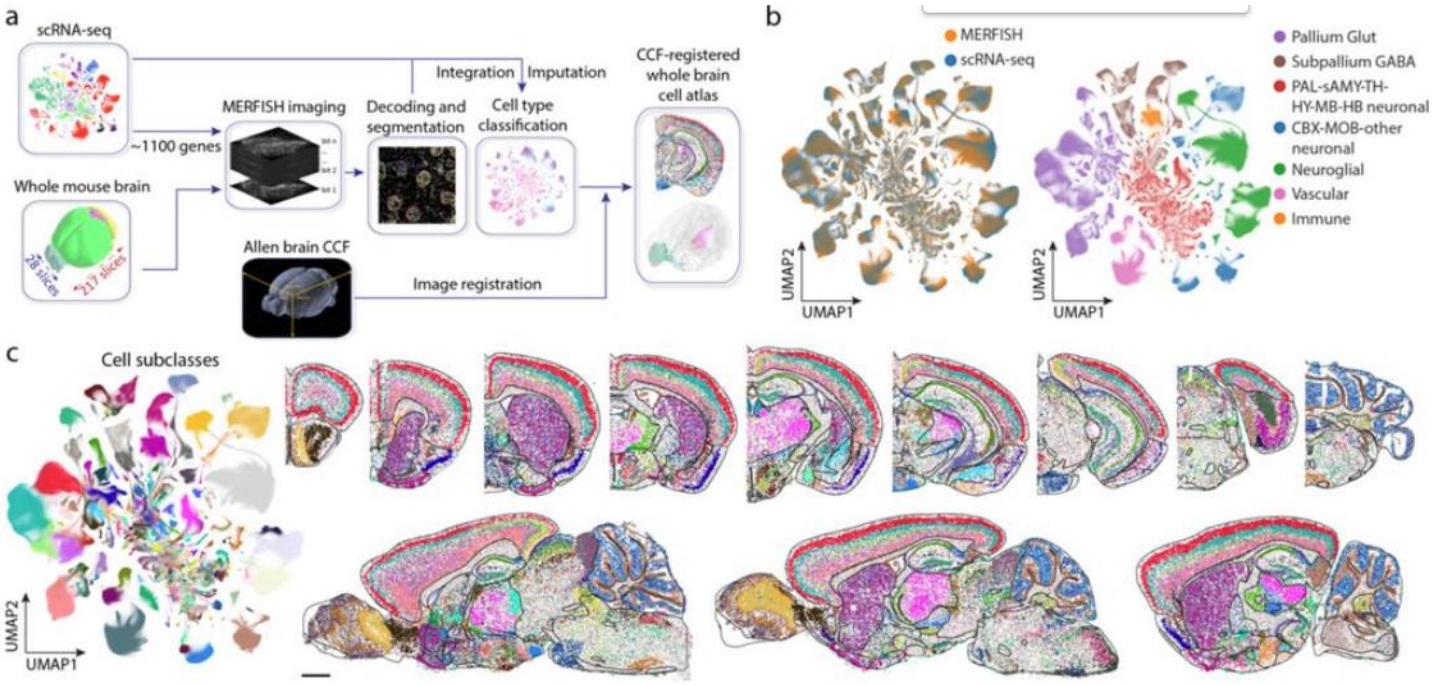

Figure 3. A molecularly definded and spatially resolved cell atlas of whole mouse brain.

This months 3rd paper is from the Zhuang group, which pioneer work in spatial transcriptomic technologies. Zhang *et al.* generated a **spatial atlas of whole mousebrain by imaging ~8 million cells**. Molecularly defined cell types across the entire mouse brain was identified, the atlas was generated using MERFISH imaging and integration with scRNA-seq data. The resulting work provides a comprehensive reference of the molecular diversity and spatial organization of cells in the mouse brain, with **>5,000 transcriptionally distinct neuronal cell clusters belonging to 283 subclasses**. Most molecularly distinct neuronal cell types exhibit distinct spatial distributions and strong enrichment within one of the 11 major brain regions. The telencephalic regions show lower diversity of cells in each region, while the hypothalamus, midbrain, and hindbrain exhibit higher cellular diversity. The spatial distributions of the transcriptionally distinct neuronal cell types allowed the brain to be divided into molecularly defined brain regions, which showed both similarities and differences to the brain regions defined in the current Allen CCF.
Non-neuronal cells account for more than half of the cells in the adult mouse brain, and the atlas revealed a remarkably high diversity of **non-neuronal cells**, **comprising ~100 transcriptionally distinct clusters belonging to 23 subclasses**. Many non-neuronal cell types exhibited a high level of regional specificity, particularly astrocytes.

The atlas also enabled a **brain-wide investigation of cell-type-specific cell-cell**. Across the whole brain, several hundred pairs of cell types were predicted to communicate in specific ways, potentially revealing the molecular basis and functional implications of these interactions.

Next Single Cell Seminar

Date TBA

Speakers

TBA

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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