DANISH SINGLE-CELL NETWORK NEWSLETTER

February - 2025

THIS MONTH'S HIGHLIGHTS:

ScaleSC: A superfast and scalable single-cell RNA-seq data analysis pipeline powered by GPU

Hu, W., Zhang, H., Sun, Y.H. et al.

Spatial Integration of multi-omics single-cell data with SIMO

Yang, P., Jin, K., Yao, Y. et al.

Simultaneous profiling of chromatin-associated RNA at targeted DNA loci and RNA-RNA Interactions through TaDRIM-seq

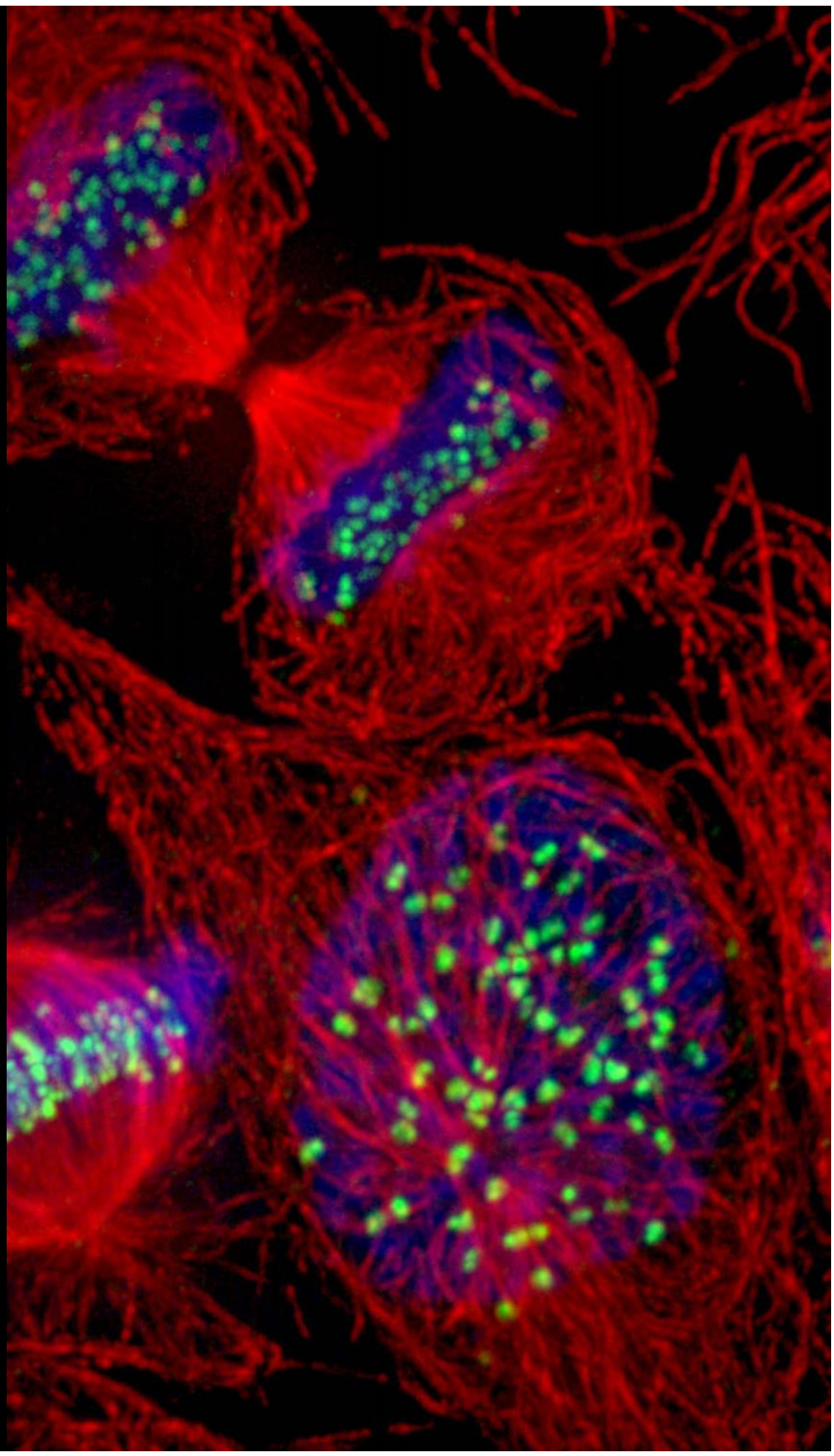
Ding, C., Chen, G., Luan, S. et al.

Massively parallel in vivo Perturb-seq screening

Zheng, X., Thompson, P.C., White, C.M. et al.

Linking single-cell transcriptomes with secretion using SEC-seq

Langerman, J., Baghdasarian, S., Cheng, R.Y. et al.



COVER IMAGE
Author: Dr. Jennifer Waters & Dr. Adrian Salic, Harvard Medical School, Department of Cell Biology, Boston, Massachusetts, USA
Title: Mitotic human cells (microtubules, kinetochores, and DNA) (2004)

UNIVERSITY OF COPENHAGEN

UPCOMING EVENT

5th Danish Single-Cell Symposium:
Technology towards Cell Biology and Medicine

https://events.au.dk/5thdanishsingle-cellsymposium/conference

Time and place: May 15th-16th 2025; Panum, University of Copenhagen

Deadline for registration: May 1st

ScaleSC: A superfast and scalable single cell RNA-seq data analysis pipeline powered by GPU

Hu, W., Zhang, H., Sun, Y.H. *et al. bioRxiv* (2025), https://doi.org/10.1101/2025.01.28.635256

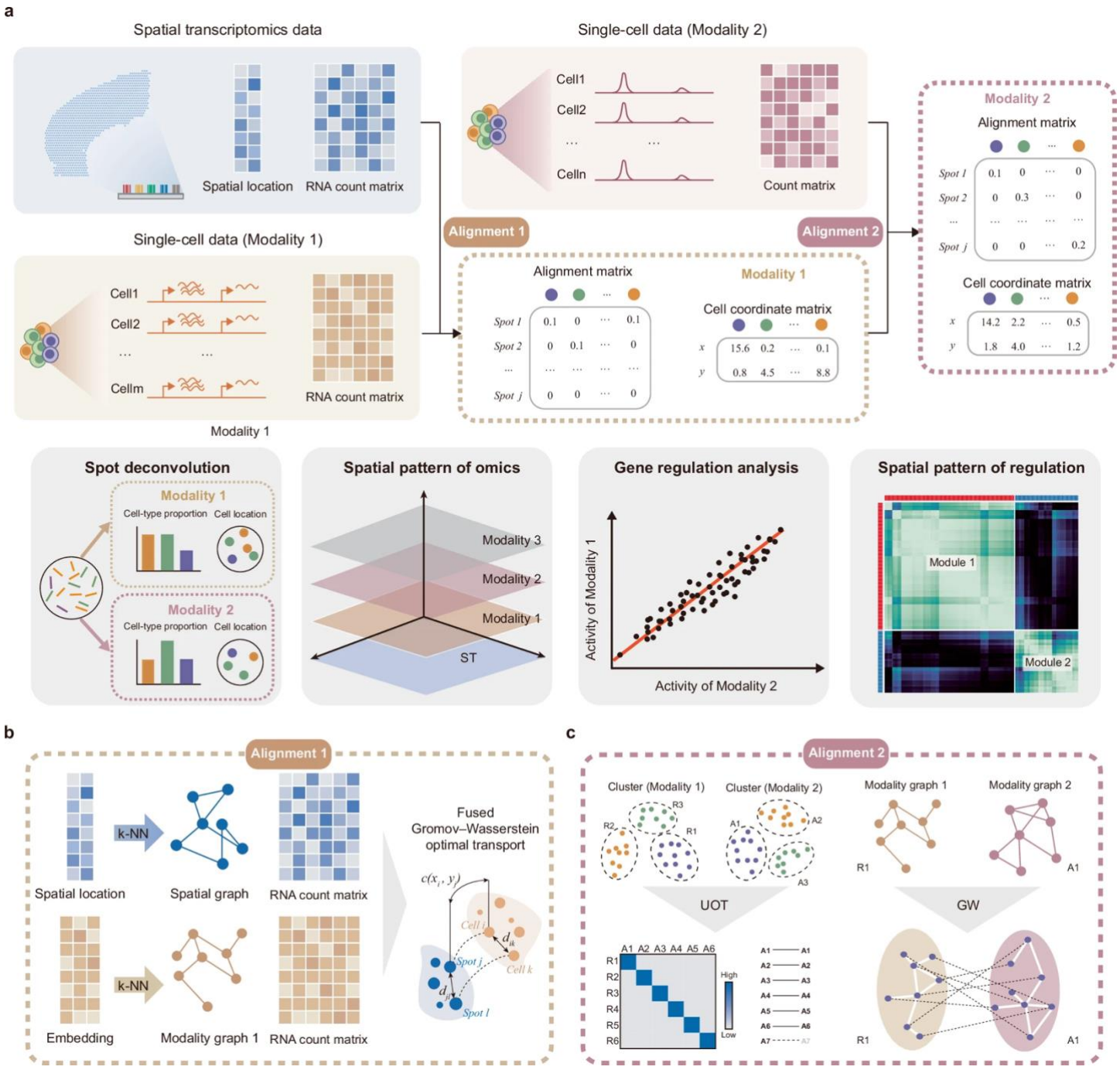
Processing large-scale scRNA-seq datasets presents significant computational hurdles, requiring both high-speed performance and scalability. **ScaleSC,** a newly developed GPU-accelerated pipeline, offers a transformative solution by providing over a 20x increase in processing speed compared to traditional CPU-based workflows. Built on Scanpy and rapids-singlecell, ScaleSC efficiently processes datasets containing 10–40 million cells, leveraging a single A100 GPU to overcome the notorious memory bottlenecks associated with high-throughput sequencing data. Importantly, ScaleSC eliminates discrepancies between GPU and CPU computational outputs, ensuring analytical consistency across different computing environments.

Beyond its core optimizations, ScaleSC introduces several advanced tools, including **high-speed marker gene identification** and **cluster merging algorithms**, both crucial for revealing biologically relevant cell subtypes and transitions. Designed with user accessibility in mind, the pipeline integrates seamlessly into existing Scanpy workflows, requiring minimal adaptation from researchers. Given its remarkable efficiency and ease of implementation, ScaleSC is poised to redefine how computational single-cell biologists process and interpret massive sequencing datasets, democratizing access to high-performance analysis for large-scale studies.

Spatial integration of multi-omics single-cell data with SIMO

Yang, P., Jin, K., Yao, Y. et al. Nature Communications (2025), https://doi.org/10.1038/s41467-025-56523-4

Recent advances in spatial transcriptomics have unlocked new opportunities for understanding tissue architecture at unprecedented resolution. However, integrating diverse single-cell modalities, such as chromatin accessibility and DNA methylation, into spatial frameworks remains a major computational challenge. Enter **SIMO** (Spatial Integration of Multi-Omics), a powerful new probabilistic alignment tool designed to bridge these technological gaps. Unlike existing methods that are largely confined to transcriptomics, SIMO enables the seamless integration of multiple omics layers, offering a **comprehensive, multimodal view of cellular regulation within its spatial context**.

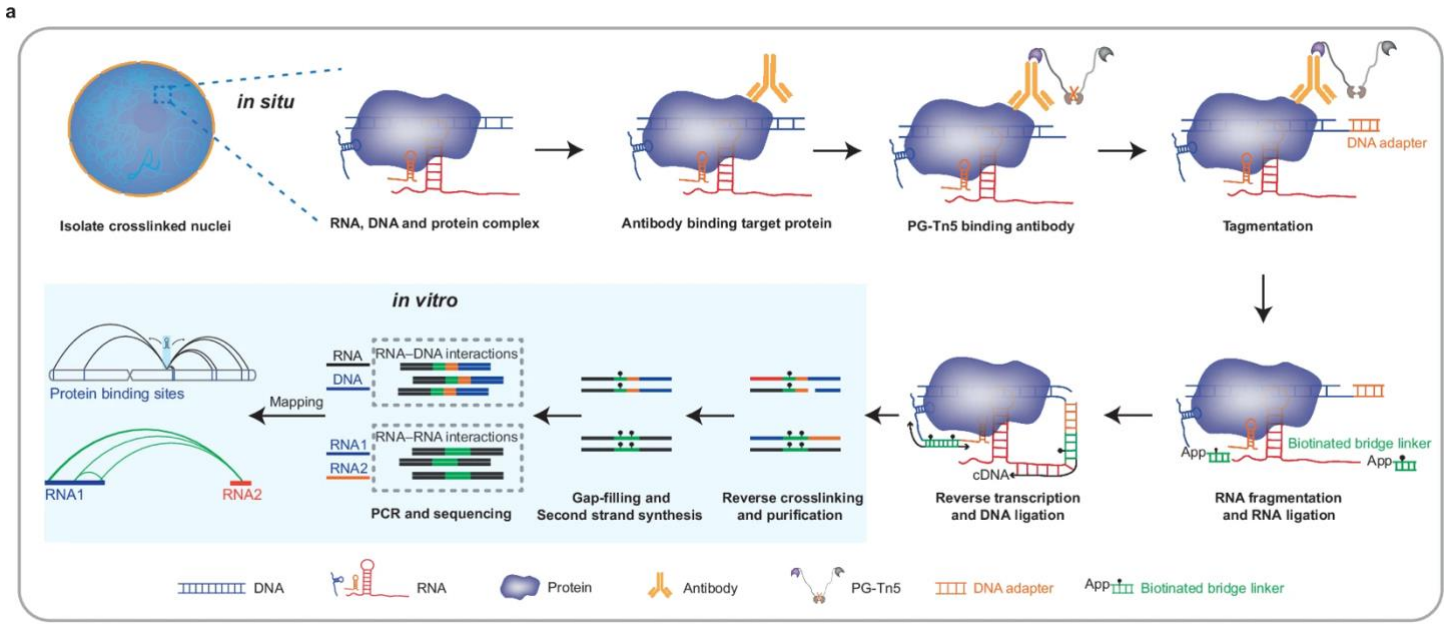


In rigorous benchmarking tests using both simulated and real-world datasets—including mouse brain and human myocardial infarction tissue—SIMO consistently outperforms traditional mapping tools. It not only accurately reconstructs spatial organization but also reveals **topological regulatory patterns that govern cellular interactions and tissue heterogeneity**. By integrating DNA methylation and chromatin accessibility with transcriptomic landscapes, SIMO provides an essential framework for studying **epigenetic regulation at a single-cell level**. Researchers using SIMO can now dissect the spatial heterogeneity of tissues with newfound clarity, making it a game-changer for developmental biology, neuroscience, and disease pathology.

Simultaneous profiling of chromatin-associated RNA at targeted DNA loci and RNA-RNA Interactions through TaDRIM-seq

Ding, C., Chen, G., Luan, S. *et al. Nature Communications* (2025), https://doi.org/10.1038/s41467-024-53534-5

Deciphering the intricate relationship between RNA and chromatin remains one of the most pressing challenges in molecular biology. **TaDRIM-seq** (Targeted DNA-associated RNA and RNA-RNA Interaction Mapping by Sequencing) is a revolutionary technique that simultaneously profiles **chromatin-associated RNAs (caRNAs) at targeted DNA loci** and **RNA-RNA interactions** within intact nuclei. By employing **Protein G (PG)-Tn5-targeted DNA elements** and **in situ proximity ligation**, TaDRIM-seq drastically reduces the need for high cell input and minimizes hands-on time, overcoming limitations of previous approaches.

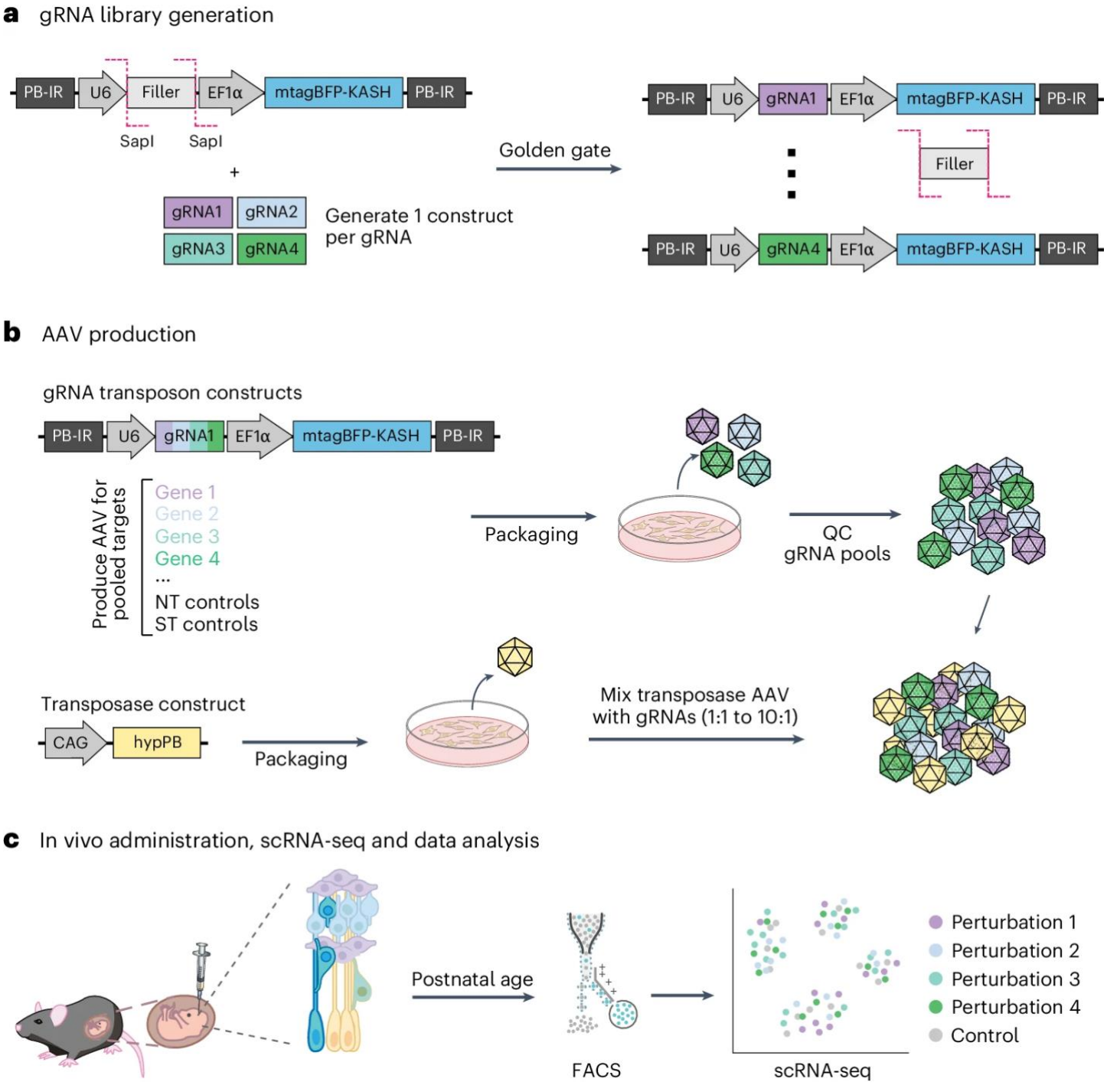


Using this technique, researchers can now map caRNAs across diverse genomic regions with **unparalleled resolution**, uncovering their roles in **gene regulation, chromatin organization, and transcriptional control**. Applied to both mammalian and plant systems, TaDRIM-seq has revealed **chromatin-associated RNAs enriched at DNA anchor points of chromatin loops**, shedding light on the dynamic nature of gene regulation. Furthermore, its ability to **capture RNA-RNA spatial interactions within nuclei** provides insights into the broader complexity of 3D genome architecture. This technique is set to transform how scientists study RNA function in genome organization and transcriptional dynamics.

Massively parallel in vivo Perturb-seq screening

Zheng, X., Thompson, P.C., White, C.M. *et al. Nature Protocols* (2025), https://doi.org/10.1038/s41596-024-01119-3

Traditional genetic perturbation screens have provided valuable insights into gene function, yet most studies remain confined to in vitro models, limiting their physiological relevance. **Massively Parallel In Vivo Perturb-seq** introduces an innovative approach that enables genome-wide functional screening in living organisms. By combining **high-throughput CRISPR-based perturbations with scRNA-seq in vivo**, this methodology allows researchers to systematically dissect gene function across multiple cell types within intact tissues.



Central to this technique is the use of **adeno-associated virus (AAV) vectors equipped with a transposon system**, enabling rapid and efficient perturbation delivery. Unlike traditional lentivirus-based delivery, AAV ensures robust gene expression modulation across diverse tissues while maintaining minimal immunogenicity. The Perturb-Seq pipeline empowers researchers to conduct **large-scale functional genomic studies in mammalian systems**, unlocking new possibilities for disease modeling, drug target identification, and developmental biology research. With its scalability and precision, this method stands to revolutionize genetic screening in live animal models.

Linking single-cell transcriptomes with secretion using SEC-seq

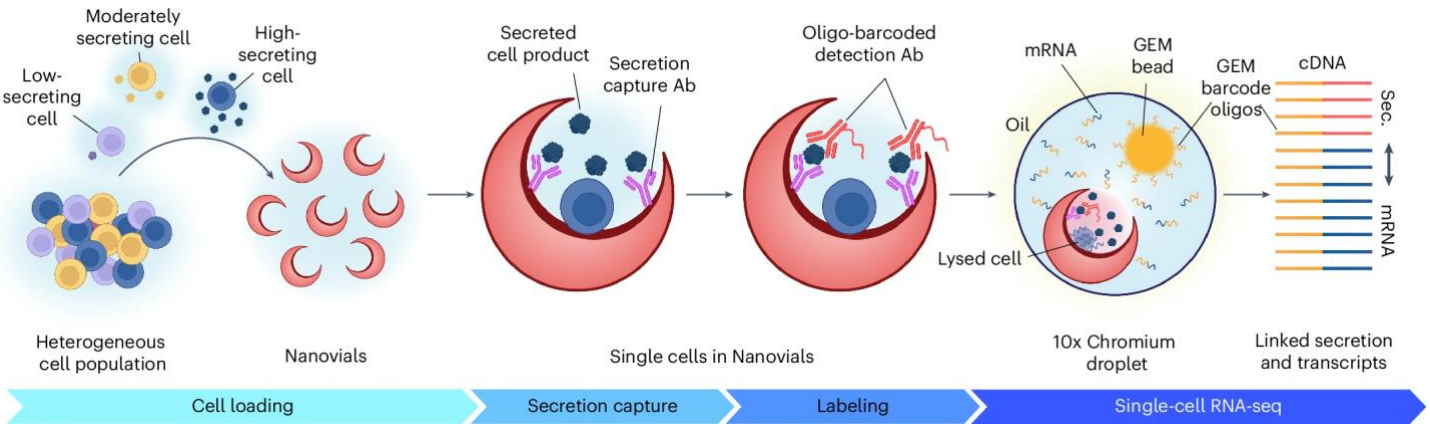
Langerman, J., Baghdasarian, S., Cheng, R.Y. *et al. Nature Protocols* (2025), https://doi.org/10.1038/s41596-024-01112-w

Cellular secretion is fundamental to immune responses, intercellular communication, and therapeutic applications, yet its precise regulatory mechanisms remain elusive. **SEC-seq** (Secretion Encoded Single-Cell Sequencing) introduces a groundbreaking method to link single-cell transcriptomes with secretion profiles. By leveraging **Nanovials—hydrogel microparticles that capture secreted proteins**, SEC-seq enables direct coupling of transcriptomic and secretory phenotypes at a single-cell resolution.

This method has been applied to various biological contexts, including:

- **T cells**, where SEC-seq identified cytokine-secreting subsets linked to specific immune responses.
- **Mesenchymal stromal cells (MSCs)**, revealing a distinct subpopulation with enhanced regenerative potential based on VEGF-A secretion.
- **Plasma cells**, demonstrating novel transcriptomic markers that correlate with high immunoglobulin secretion.

By providing a **spatiotemporal link between gene expression and secretion phenotypes**, SEC-seq paves the way for new discoveries in immunology, regenerative medicine, and biotechnology. This technology holds immense promise for optimizing cell-based therapies and uncovering novel biomarkers of functional cellular states.



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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