DANISH SINGLE-CELL NETWORK NEWSLETTER

NOVEMBER/DECEMBER - 2024

THIS MONTH'S HIGHLIGHTS:

Leveraging deep single-soma RNA sequencing to explore the neural basis of human somatosensation
Yu, H., Nagi, S.S., Usoskin, D. et al

scPair: Boosting single cell multimodal analysis by leveraging implicit feature selection and single cell atlases Zhang, Hu, H., Quon, G

Single-cell RNA sequencing of terminal ileal biopsies identifies signatures of Crohn's disease pathogenesis Simon, Krzak, M., Alegbe, T., Taylor, D.L., Jones G., et al

Spatiotemporal single-cell roadmap of human skin wound healing
Liu, Z., et al

COVER IMAGE
Jamie Whitelaw, University of the West of Scotland/CRUK Beatson Institute:

The images were processed to form an Xmas tree where the actin staining is the tree, the DAPI is baubles and the Vinculin as the Xmas lights. (2022)

UNIVERSITY OF COPENHAGEN

Leveraging deep single-soma RNA sequencing to explore the neural basis of human somatosensation

Yu, H., Nagi, S.S., Usoskin, D. et al.. *Nature Neuorscience* (2024)
https://doi.org/10.1038/s41593-024-01794-1

How do our nerves detect pain, temperature, or touch? Single-cell sequencing is helping scientists answer this question by studying dorsal root ganglion (DRG) neurons—key players in our sensory system. These neurons have been difficult to study because it's hard to separate them from surrounding cells. One powerful technique used in this study is deep single-soma RNA sequencing, which involves isolating and sequencing RNA from the cell body of a single neuron. This method allows researchers to capture the unique gene expression profiles of individual neurons with great precision. By combining this approach with advanced tools like Laser Capture Microdissection (LCM), Smart-seq2, and 10x Xenium spatial transcriptomics, scientists analyzed DRG neurons in incredible detail. They discovered unique neuron types, which likely senses mechanical signals in blood vessels and organs, and showed how certain molecules control heat and cold sensitivity. These findings highlight how single-cell methods can reveal the complexity of our sensory system.

This study also demonstrated how combining single-cell and spatial techniques creates a more complete picture of DRG neurons. Spatial transcriptomics showed that neurons of the same type tend to cluster together in patterns, likely reflecting their development. Meanwhile, deep single-soma RNA sequencing helped classify neurons more accurately by capturing subtle differences in their gene expression. These tools not only reveal how our nerves function but also offer insights into changes that occur in diseases like chronic pain. By expanding these methods to study neurons from different body regions and conditions, scientists can uncover new targets for treating sensory disorders and improving our understanding of the nervous system.

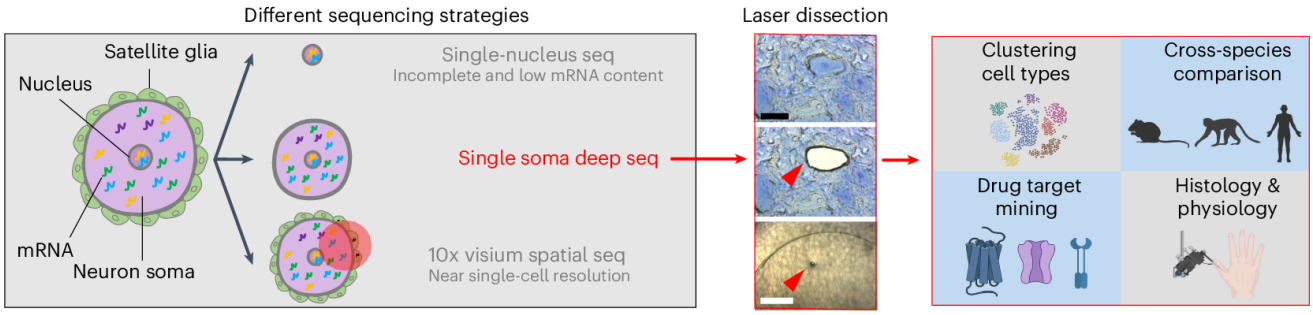


Figure 1. Overall workflow of this study. Left, features associated with different strategies for single-cell RNA-seq of hDRG neurons. Middle, example of the laser dissection of an hDRG neuron soma. Right, summary of analyses and experiments. Scale bar, 50 µm (cell) and 500 µm (cap).

scPair: Boosting single cell multimodal analysis by leveraging implicit feature selection and single cell atlases

Hu, H., Quon, G. *Nature Communications* (2024),
https://doi.org/10.1038/s41467-024-53971-2

scPair is a new deep learning tool that helps researchers analyze single-cell multimodal data, like RNA and ATAC sequencing. It works by automatically finding the most important features in each dataset to map cell states between different data types. Unlike older methods that rely on pre-selecting features based on variance, scPair learns directly from the data to figure out what matters most. It also uses large single-modality datasets, which are often higher quality, to improve its understanding of patterns and make more accurate predictions. This makes scPair great for tasks like mapping cell states, predicting features, and studying how cells change over time.

What makes scPair different is that instead of simply compressing data into a smaller format, it trains each dataset to predict the other, which improves mapping accuracy. It avoids relying on prior knowledge, like which DNA regions regulate which genes, making it more flexible. scPair has been tested on datasets like Patch-seq and CITE-seq and could be expanded to work with imaging or sequence data in the future. While it does require some paired multimodal data, scPair provides a more accurate and adaptable way to study complex cell types and low-throughput datasets, offering new opportunities in single-cell research.

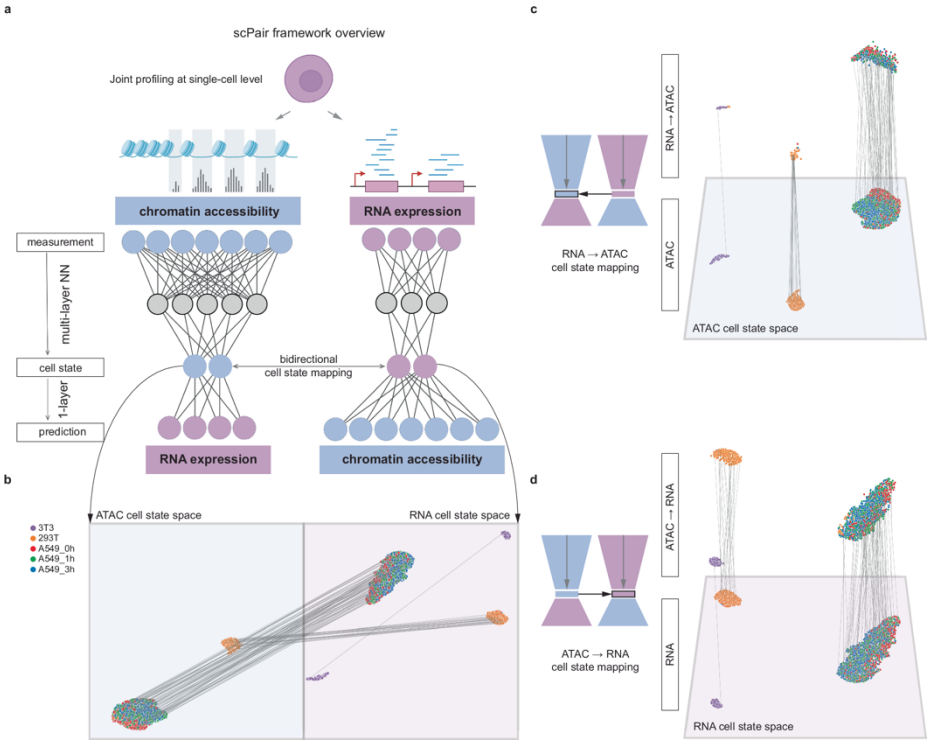
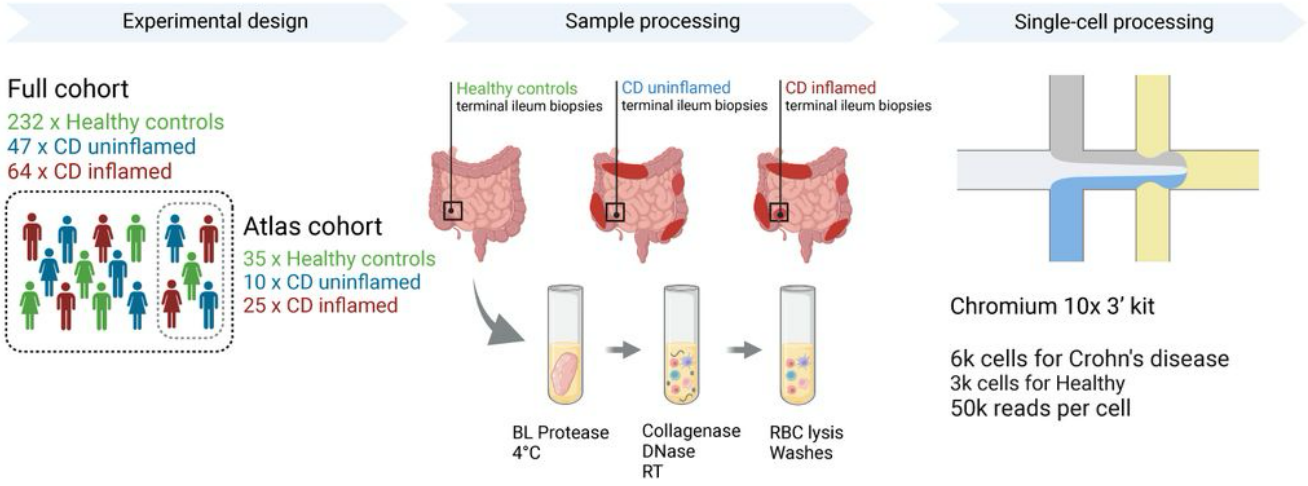


Figure 2. (a) scPair uses dual feedforward networks to predict each modality from the other, with the last hidden layer encoding modality-specific cell state spaces. (b) UMAP visualization of modality-specific cell states from scPair, colored by original cell type labels, with lines connecting states of the same cell. (c) scPair's bidirectional mapping: RNA profile predicts ATAC cell state (top), compared to ground truth (bottom), with prediction accuracy shown by vertical lines. (d) Same as (c), but predicting RNA state from ATAC.

Single-cell RNA sequencing of terminal ileal biopsies identifies signatures of Crohn's disease pathogenesis

Krzak, M., Alegbe, T., Taylor, D.L., Jones G., et al . *medRxiv* (2024),
https://doi.org/10.1101/2023.09.06.23295056

IBDverse is a groundbreaking resource for studying Crohn's disease (CD), offering the largest single-cell RNA sequencing dataset of terminal ileum biopsies to date. With over 1.1 million cells from 343 patients, including 111 with CD and 232 healthy controls, this comprehensive dataset provides crucial insights into the molecular landscape of CD, a complex inflammatory bowel disease.



The study highlights significant findings, including a key role for ITGA4+ macrophages in CD. These immune cells contribute to inflammatory pathways, such as JAK/STAT signaling, making them potential targets for future treatments. The dataset also shows how immune cells are involved in disease progression, offering new opportunities for therapeutic intervention.

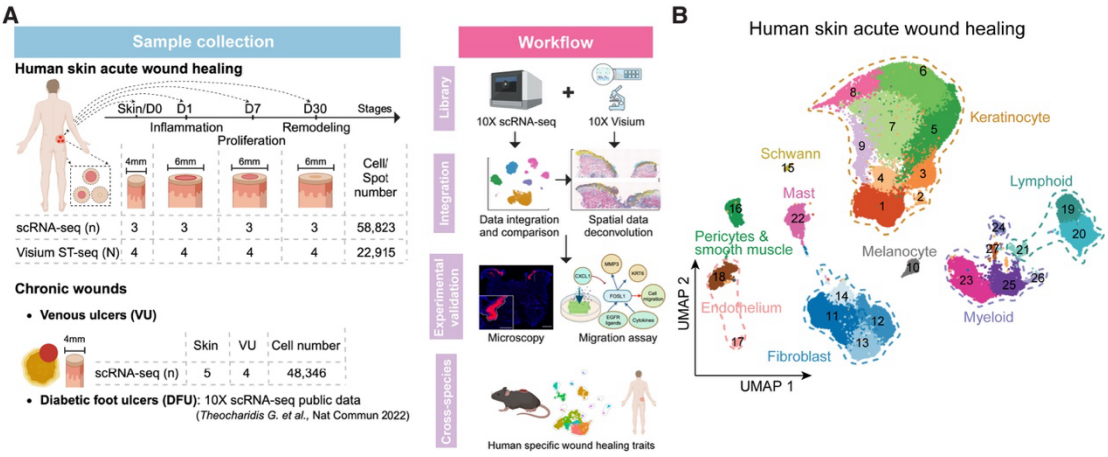
IBDverse also focuses on changes in epithelial cells, which form the barrier between the gut and the rest of the body. These cells show persistent changes due to Type I and Type II interferon signaling, suggesting that inflammation can leave lasting molecular effects even after the disease seems to be under control.

In addition to its findings, IBDverse is an open-access resource that can help researchers better understand the mechanisms behind CD. By providing detailed insights into immune responses, epithelial biology, and genetic factors, this dataset offers an important foundation for advancing CD research and therapy. With IBDverse, researchers can explore new ways for targeting CD, potentially improving treatments and outcomes for patients.

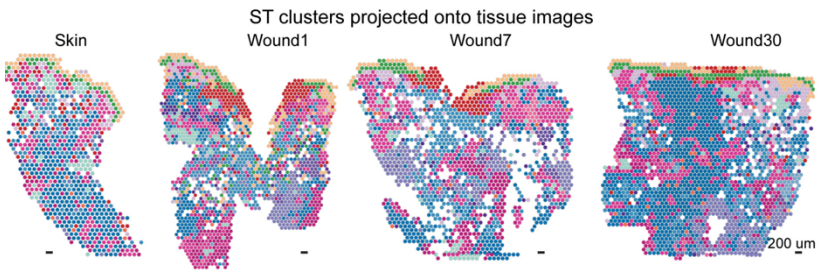
Spatiotemporal single-cell roadmap of human skin wound healing

Liu, Z., et al . *Cell Stem Cell* (2024),
https://doi.org/10.1016/j.stem.2024.11.013

This study introduces a spatiotemporal cell atlas of human skin wound healing, built using scRNA-seq and ST-seq to track gene expression at the single-cell level during different healing stages. The interactive atlas, available online (https://www.xulandenlab.com/tools), allows users to explore key insights into wound healing, including the mechanisms driving re-epithelialization and comparisons between acute and chronic wounds. It also compares human and mouse wound healing, showing both shared and distinct healing processes, offering a valuable tool for translating basic research into treatments.



Wound healing involves complex coordination between various cells and signals, often studied in animal models. To better understand how these processes work in humans, this study uses a human wound-healing model, providing detailed views of cellular changes throughout healing. It focuses on re-epithelialization and the key molecular networks that help keratinocytes move, which is essential for skin repair. The study also examines differences between chronic and acute wounds, identifying potential treatment targets.



This study offers a valuable resource for understanding wound healing and provides a new perspective on treating chronic wounds, with the interactive atlas helping to drive further discoveries and collaborations in the field. However, it has some limitations, including the lack of single-cell resolution in some data and the limited sampling of wounds at only a few time points. More research with higher resolution and larger datasets will be needed to confirm these findings, especially for chronic wounds.

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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