Single Cell Sequencing for Healthy Longevity Research

Introduction

Background: A rapidly aging population increases the burden of age-related diseases, making it critical to understand the cellular mechanisms driving decline.

Challenge: Aging manifests differently across cell types and tissues, requiring resolution of cellular heterogeneity.

Relevance of Single Cell Analysis: Provides cellular-level insights to uncover biomarkers, reveal drug targets, and guide interventions that promote healthy aging.

How Single Cell Sequencing Contributes to Healthy Longevity Research

- **Identify** cell populations driving age-related pathology
- **Resolve** cell-type-specific molecular signatures
- **Track** clonal dynamics over time
- **Map** altered cell–cell communication networks

Single Cell Analysis Workflow

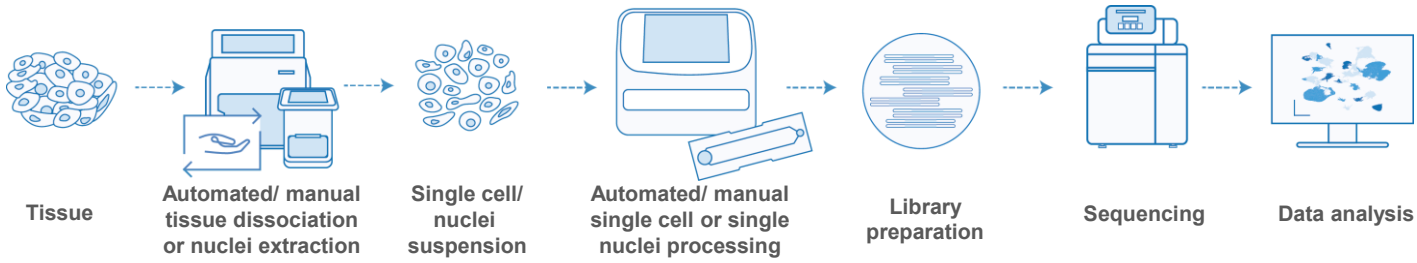

Figure 1: Single cell analysis workflow

Applications of Single Cell Analysis in Healthy Longevity Research

Single cell sequencing technologies address critical research questions.

1. Age-related disease mechanisms

Linking cellular features to neurodegenerative diseases, cancer susceptibility, and metabolic disorders

2. Aging and immunology

Characterizing immune cell sub-population changes and inflammatory profiles

3. Tissue-specific impact of aging

Mapping transcriptional and epigenetic changes in brain, muscle, and other organs

4. RNA turnover rates in aging

Measuring transcriptional dynamics and identifying age-related changes in transcriptome activity

1. Aging-related Disease Mechanisms

Aging-related diseases affect billions worldwide. Single cell sequencing provides an unbiased view of cell types and phenotypes involved in disease conditions, and can be used to:

- Reveal cell type distributions in disease vs. control
- Identify differential gene expressions
- Predict potential therapeutic targets

Case study: Parkinson's Disease (PD) Neuroinflammation

Scan to read it in *Signal Transduction and Targeted Therapy* →

Mirzac et al. (2025) constructed a first single cell genomic map of the human PD cortex. By profiling 101,691 cells from 14 dorsolateral prefrontal cortex samples, they identified:

- Molecular dysregulation in four main cell types, especially in metabolic and cerebrovascular mechanisms.
- Using gene-drug interaction analysis, they identified five potential drug candidates against upregulated genes.

Data Showcase:

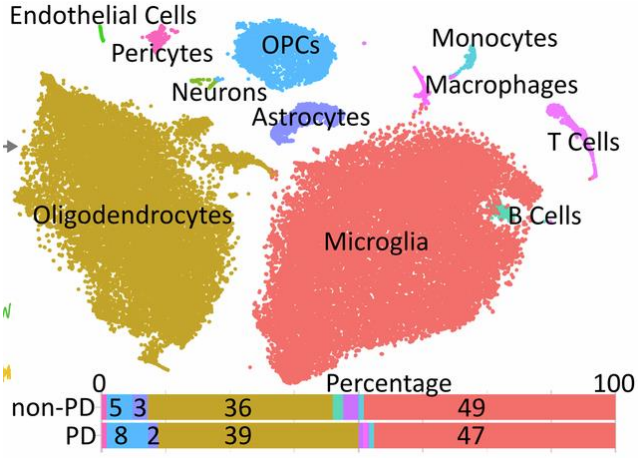

Figure 2. t-SNE map with bar plot distribution by percentage of the identified cell types between cohorts. Image from Mirzac et al. (2025). CC BY 4.0.

Case study: Analysis of PD patient-derived organoids

Scan to read it in *npj Parkinson's Disease* →

Zagare et al. (2025) generated an scRNA-seq dataset of patient-derived midbrain organoids to decipher shared dysregulation across PD variants. Network-based analysis revealed:

- PD patient iPSC-derived organoids showed reduced dopaminergic neuron populations and differential gene expression.
- ROBO signaling may play an important role in PD.
- The identified signatures could serve as biomarkers for patient stratification.

Data Showcase:

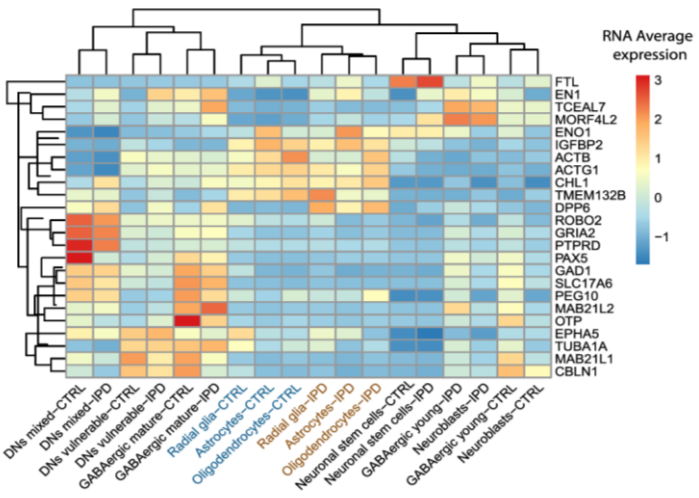

Figure 3. Unsupervised clustering of cells from PD and control samples based on the average expression of 25 genes of interest. Image from Zagare et al. (2025). CC BY 4.0.

Case Study: Single Cell Analysis of Clonal Hematopoiesis

Scan to learn more at *singleron.bio* →

Clonal hematopoiesis of indeterminate potential (CHIP) involves age-related accumulation of somatic mutations in hematopoietic stem cells, leading to clonal expansion. CHIP is associated with increased risk of malignancies and other conditions.

The FocuSCOPE® Clonal Hematopoiesis kit enables researchers to detect five common CHIP mutations (Table 1) in addition to the full transcriptome, providing insights into the molecular mechanisms of CHIP-related diseases and the aging process.

Gene	Description
DNMT3A	DNA methyltransferase
TET2	DNA-binding protein
ASXL1	Chromatin binding protein
TP53	Transcription factor
JAK2	Protein tyrosine kinase

Table 1. CHIP mutations covered by the FocuSCOPE Clonal Hematopoiesis single cell sequencing kit.

Data Showcase:

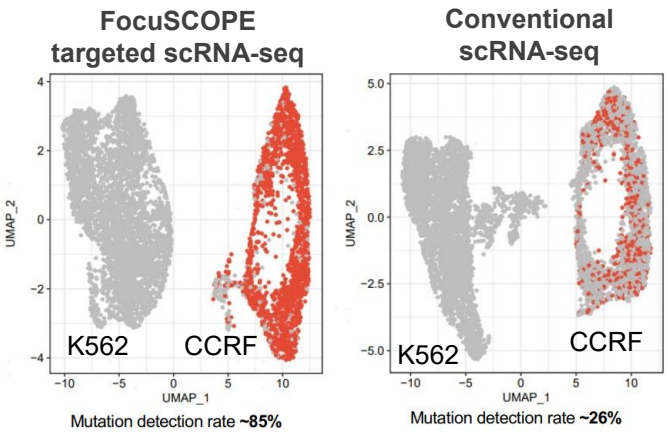

Figure 4. FocuSCOPE detects TP53 mutation at higher sensitivity than conventional scRNA-seq. CCRF (contains TP53 mutation R248Q) and K562 (negative control) cell lines were mixed in equal proportions. Libraries were prepared either with FocuSCOPE or with conventional single cell sequencing kits. Red: R248Q mutation detected.

Digital Twins for Healthy Longevity

AD-Omics is a collaboration between the Institute for Healthy Living Abu Dhabi (IHLAD) and Singleron, using single cell multi-omics and AI to create digital twins that improve personalized healthcare and healthy longevity.

Learn more here: https://adomics.ae/

AD-OMICS

References

Mirzac, D., Bange, M., Kunz, S., et al. (2025). Targeting pathological brain activity-related to neuroinflammation through scRNA-seq for new personalized therapies in Parkinson's disease. *Signal Transduction and Targeted Therapy*, *10*, 10. https://doi.org/10.1038/s41392-024-02086-7

Zagare, A., Balaur, I., Rougny, A., et al. (2025). Deciphering shared molecular dysregulation across Parkinson's disease variants using a multi-modal network-based data integration and analysis. *npj Parkinson's Disease*, *11*, 63. https://doi.org/10.1038/s41531-025-00914-3

2. Aging and Immunology

Aging leads to profound alterations in the immune system, which increase susceptibility to diseases. Single cell sequencing can help identify changes in:

immune cell proportions

immune cell status (activation, exhaustion, etc.)

clonality and cell-cell interactions

Case study: ECM Degradation-Induced Immune Changes

Scan to read it in *Nature Aging* →

Yi et al. (2025) investigated the role of extracellular matrix (ECM) degradation in aging. They identified an increase in the level of serum elastin fragments. Elastin fragment injection reduced healthspan in mice.

scRNA-seq on sorted T/B cells from the spleen of mice treated with an elastin-derived peptide revealed:

- Immune cell activation, with upregulation of proinflammatory genes in T cells.
- Cell-type-specific responses: The treatment increased T cell subpopulations including cytotoxic T cells and regulatory T cells.
- NEU1 was identified as responsible for elastin fragment-induced inflammation, and its inhibition extends mouse healthspan.

Data showcase:

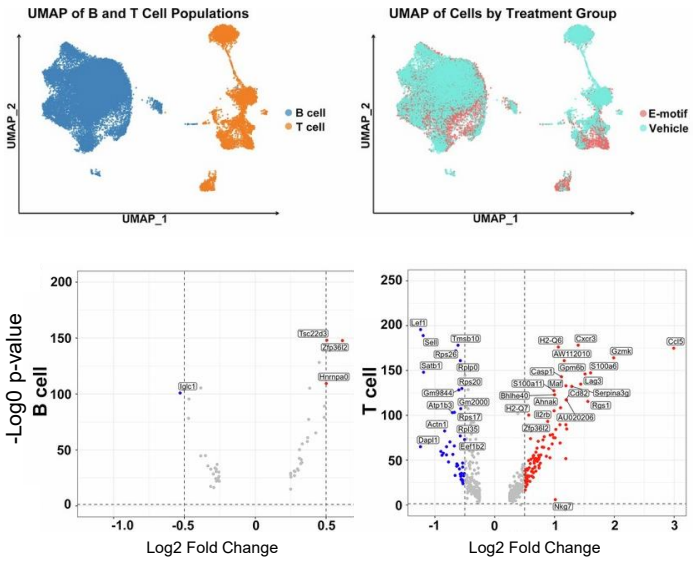

Figure 5. Top: UMAP plots of all cells colored by cell type (T cells vs. B cells, left) and by treatment group (E-motif vs. vehicle, right). Bottom: Volcano plots showing differentially expressed genes (DEGs) between vehicle and E-motif groups for T cells and B cells, respectively. Image from Yi et al. (2025). CC BY 4.0.

Reference

Yi, J., Wang, Y., Sui, H., et al. (2025). Elastin-derived extracellular matrix fragments drive aging through innate immune activation. *Nature Aging*. https://doi.org/10.1038/s43587-025-00961-8

3. Tissue-specific Impact of Aging

Aging does not affect tissues uniformly. Different organs may experience various impacts, such as the pancreas, lung, liver, and skeletal muscle. Single cell sequencing can reveal tissue-specific phenotypes and the underlying cellular changes, with some cell populations showing preserved proportions, while others undergo dramatic shifts

Case study: Transcriptional Diversity in Muscle Aging

Scan to read it in *Aging Cell* →

Liu et al. (2025) investigated transcriptional responses to aging across different skeletal muscle types using scRNA-seq. scRNA-seq uncovered heterogeneous aging responses across muscle groups as well as non-muscle cell types, challenging the notion of uniform skeletal muscle aging. Key findings include:

- The main cell-type compositions are largely unchanged with aging.
- However, changes were observed in myonuclei subtypes. Type II myonuclei showed particular sensitivity to aging.
- Pathway analysis identified downregulation of metabolic pathways associated with neuromuscular diseases
- Ligand-receptor analysis revealed a key role for EGF. An EGFR inhibitor partially reversed EGF-induced changes, suggesting a potential therapeutic target.

Data Showcase:

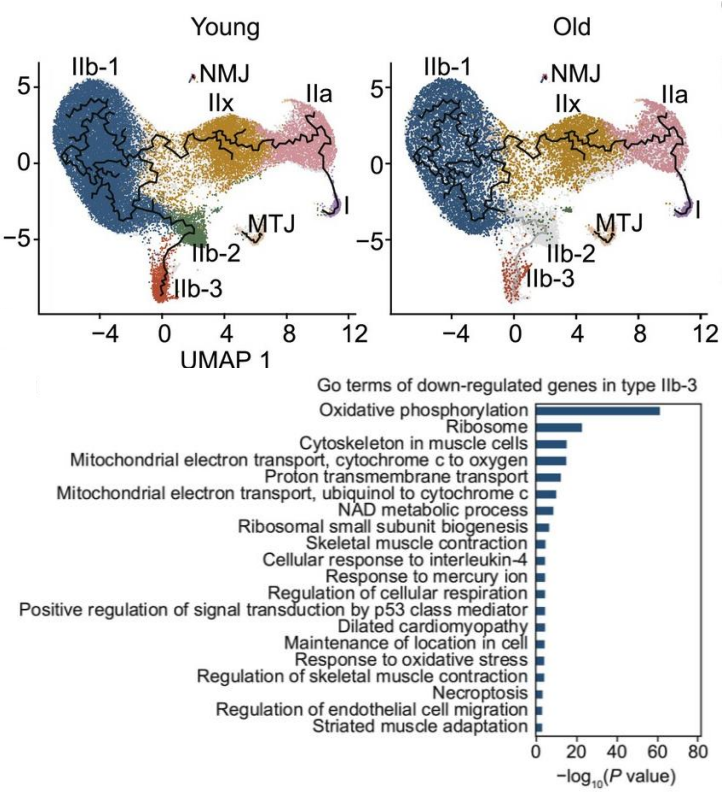

Figure 6. Top: UMAP visualization of myonuclear trajectory in young and old groups. Myonuclei are color-coded by subtype. Bottom: Gene ontology (GO) terms and KEGG pathways of downregulated genes in type IIb-3 myonuclei. Image from Liu et al. (2025). CC BY 4.0.

Reference

Liu, C., Zheng, D., Zhang, R., et al. (2025). Transcriptional diversity in response to aging across skeletal muscles. *Aging Cell*, *24*(9): e70164. https://doi.org/10.1111/acel.70164

4. Aging and Transcriptome Dynamics

Aging impacts not only RNA expression levels but also how rapidly new mRNAs are generated.

Using S^{4}U labeling, the Singleron DynaSCOPE® kit helps distinguish newly generated transcripts from the existing ones, providing an overview of the RNA turnover rate of individual genes at the single-cell level.

Case study: Age-related RNA turnover rate in mice

Scan to learn more at *singleron.bio* →

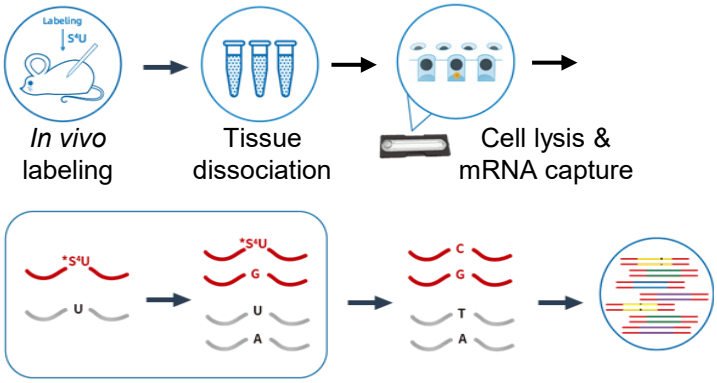

Figure 7. The DynaSCOPE workflow. A nucleotide analogue is added and incorporated into newly synthesized RNA. This results in a sequencing library with a thymine to cytosine conversion in cDNA of nascent RNA, and with a thymine in stable transcripts..

Data showcase:

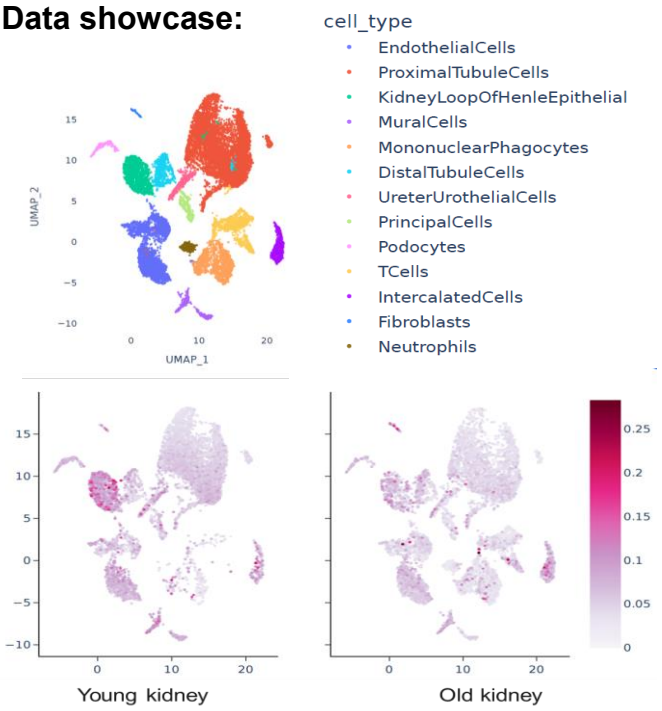

Figure 8. DynaSCOPE revealed reduced mRNA turnover in the old mouse kidney. UMAP plots of single cell sequencing data from young and old mouse kidney samples colored by cell type annotation (top) or transcriptional synthesis rates (bottom). The young mouse kidney showed more active mRNA turnover at the thick ascending limb of the loop of Henle.

Conclusion

Single cell multi-omics analysis supports healthy longevity research by revealing the cellular and molecular heterogeneity underlying aging processes. The studies presented demonstrate applications across multiple aging-relevant systems.

As the field advances towards personalized longevity interventions, single cell analysis will be essential for stratifying individuals based on cellular aging profiles and tailoring treatments to specific aging mechanisms.

EUROPE
Singleron Biotechnologies GmbH
+49 (0) 221 16824777
Gottfried-Hagen-Strasse 60
51105 Cologne, Germany
info@singleron.bio

ASIA-PACIFIC
Singleron Biotechnologies Pte. Ltd
+65 6990 5987
#02-08, 61 Science Park Rd,
Singapore 117525
sales.sg@singleron.bio

NORTH AMERICA
Singleron Biotechnologies Inc.
+1 203-298-0604 (CT)
+1 734-249-0883 (MI)
1 Bradley Road, Suite 401 Woodbridge, CT 06525
333 Jackson Plaza, Ann Arbor, MI 48103