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Development and function of mammalian tissues and organs depends on the behaviors and dynamics of individual cells. The Cao lab investigates how a cell population in a mammalian body maintains homeostasis and how it is disrupted in aging and aging-related disorders, such as Alzheimer's disease and cancer, by developing genomic techniques to profile and perturb cell dynamics at single-cell resolution.

Individual cells are the fundamental unit of form and function in biological systems. A delicately balanced program of cell proliferation, differentiation, and apoptosis ensures that tissues and organs can maintain a stable size and function throughout life. Disruptions in this homeostasis can lead to aging-related disorders, such as neurodegenerative diseases and cancer.

The Cao lab is dedicated to characterizing various aspects of single-cell biology, aiming to understand how complex cell populations maintain homeostasis in entire mammalian organisms and how this balance is disrupted in aging and aging-related diseases. To achieve this, his group develops techniques for comprehensive profiling of cell state changes over time *in vivo* and studies how cells shape and are shaped by their environments.

The first focus of Cao lab is developing exponentially scalable technologies to profile cellular dynamics and associated genomic features at a single-cell resolution. One such technology, EasySci, enables routine scanning of gene expression and chromatin accessibility profiles from millions of single cells. Applying this to human and mouse brains, his group has gained insights into gene regulation and cell population dynamics in aging and Alzheimer's disease. Another tool, TrackerSci, profiles gene expression and epigenome changes affecting progenitor cell proliferation and differentiation dynamics *in vivo*. This technique quantifies aging and Alzheimer's disease-associated shifts in cell-type-specific dynamics, deciphering associated molecular programs.

Although current single-cell genomic techniques offer comprehensive profiling of cell states, strategies for manipulating cell states and population dynamics *in vivo* are still lacking. Another goal of Cao's lab is to develop methods for cell type-specific manipulation in order to investigate the rules governing cellular functions and cell population homeostasis *in vivo*. One of these tools, PerturbSci-Kinetics, captures single-cell transcriptional dynamics in response to pooled CRISPR screens targeting various biological processes. This high-throughput technique characterizes elements that govern cell-type-specific gene regulation during RNA synthesis, processing, and degradation. This enables systematic decoding of the genome-wide regulatory network underlying cell-type-specific molecular homeostasis at scale. Additionally, his lab focuses on identifying cell-type-specific regulatory modules, such as combinations of enhancers and promoters that direct gene expression in a cell-type-specific manner. They aim to leverage this knowledge to develop tools that enhance cell population robustness or restore cell population homeostasis in aging and aging-related diseases such as Alzheimer's disease and cancer.

EDUCATION

B.S. in biological science, 2010
Peking University

Ph.D. in molecular and cellular biology, 2019
University of Washington

POSTDOC

University of Washington, 2019–2020

POSITIONS

Assistant Professor, 2020–2025
Associate Professor, 2026–
The Rockefeller University

AWARDS

Verna Chapman Young Scientist Award, 2018
Western Association of Graduate Schools and University Microfilms International Outstanding Innovation in Technology Award, 2020
Science & SciLifeLab Prize for Young Scientists, 2020
Irma T. Hirsch/Monique Weill-Caulier Trust Research Award, 2021
Sagol Network GerOmic Award for Junior Faculty, 2021
NIH Director's New Innovator Award, 2021
Melanoma Research Alliance Young Investigator Award, 2022
William Ackman and Neri Oxman Innovation Fund Award, 2022
Revolution/AFAR New Investigator Award, 2025

SELECTED PUBLICATIONS

Zhang, Z. et al. A panoramic view of cell population dynamics in mammalian aging. *Science* 387, eadn3949 (2025).
Lu, Z. et al. Tracking cell-type-specific temporal dynamics in human and mouse brains. *Cell* 186, 4345–4364 (2023).
Sziraki, A. et al. A global view of aging and Alzheimer's pathogenesis-associated cell population dynamics and molecular signatures in human and mouse brains. *Nat. Genet.* 55, 2104–2116 (2023).
Xu, Z. et al. Dissecting key regulators of transcriptome kinetics through scalable single-cell RNA profiling of pooled CRISPR screens. *Nat. Biotechnol.* (2023).
Huang, X. et al. Single-cell, whole-embryo phenotyping of mammalian developmental disorders. *Nature* 623, 772–781 (2023).