SD-NSC HETEROGENEITY OF AGING CORE

SPATIAL –OMICS AT SALK AND SANFORD BURNHAM PREBYS

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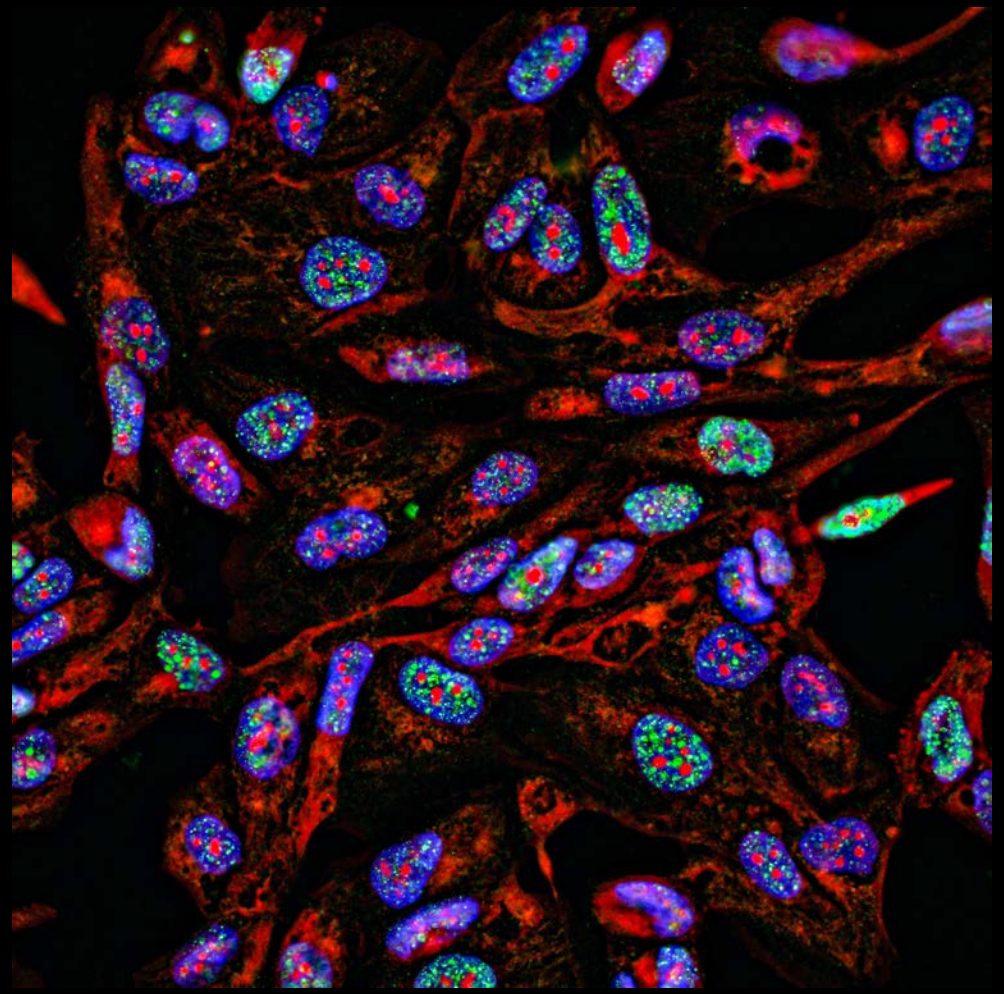


SAN DIEGO NATHAN SHOCK CENTER
2022 WORKSHOP

salk Where cures begin. | Sanford Burnham Prebys | UC San Diego School of Medicine

Why spatial –omics?

Cell – cell heterogeneity increases with age

1. Bahar et al., **Increased cell-to-cell variation in gene expression in ageing mouse heart.** Nature, 2006.

2. Martinez-Jimenez et al., **Aging increases cell-to-cell transcriptional variability upon immune stimulation.** Science, 2017.

2. Enge et al., **Single-Cell Analysis of Human Pancreas Reveals Transcriptional Signatures of Aging and Somatic Mutation Patterns.** Cell, 2017.

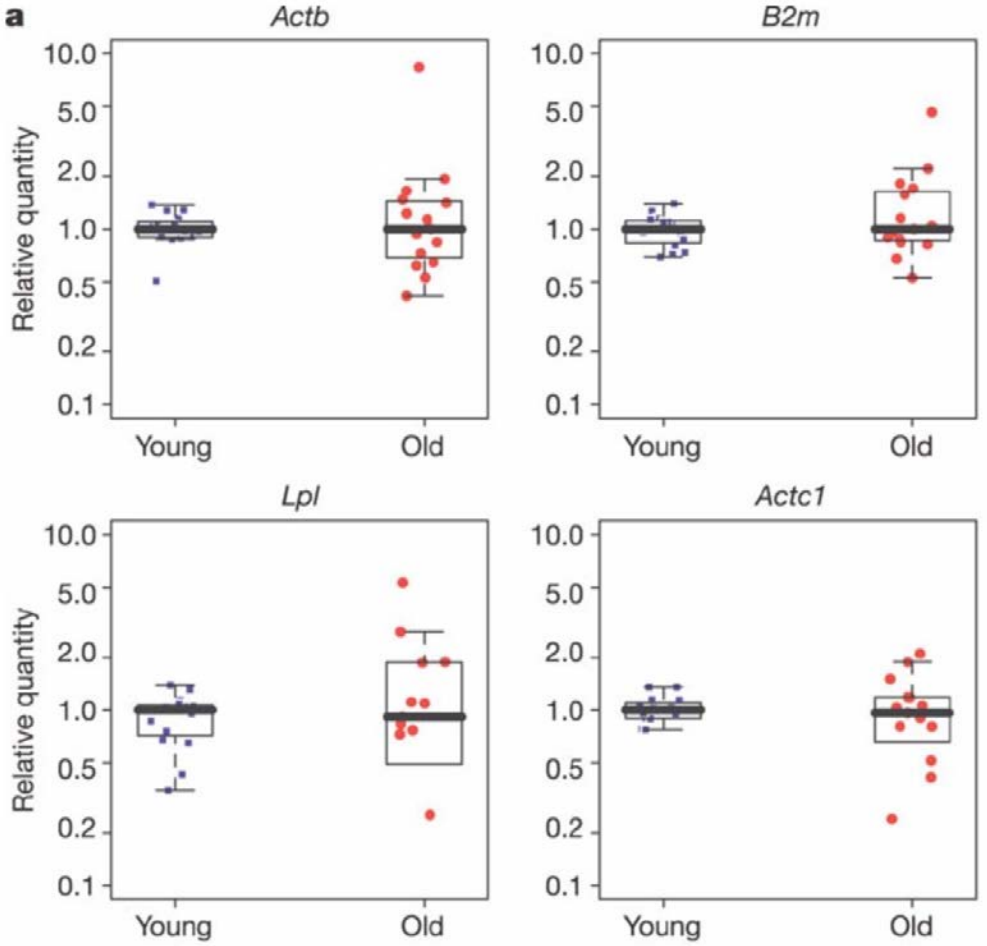
3. Cheung et al., **Single-Cell Chromatin Modification Profiling Reveals Increased Epigenetic Variations with Aging.** Cell, 2018.

4. Angelidis et al., **An atlas of the aging lung mapped by single cell transcriptomics and deep tissue proteomics.** Nat Commun, 2019.

5. Gravina et al, **Single-cell genome-wide bisulfite sequencing uncovers extensive heterogeneity in the mouse liver methylome.** Genome Biol, 2016.

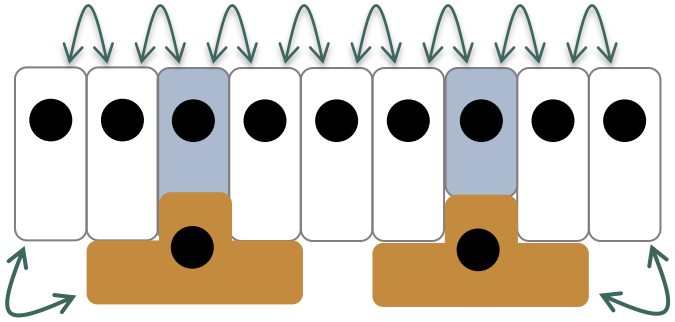
6. Hernando-Herraez et al, **Ageing affects DNA methylation drift and transcriptional cell-to-cell variability in muscle stem cells.** Nat Commun, 2019.

Increased cell-to-cell variation in gene expression in ageing mouse heart.

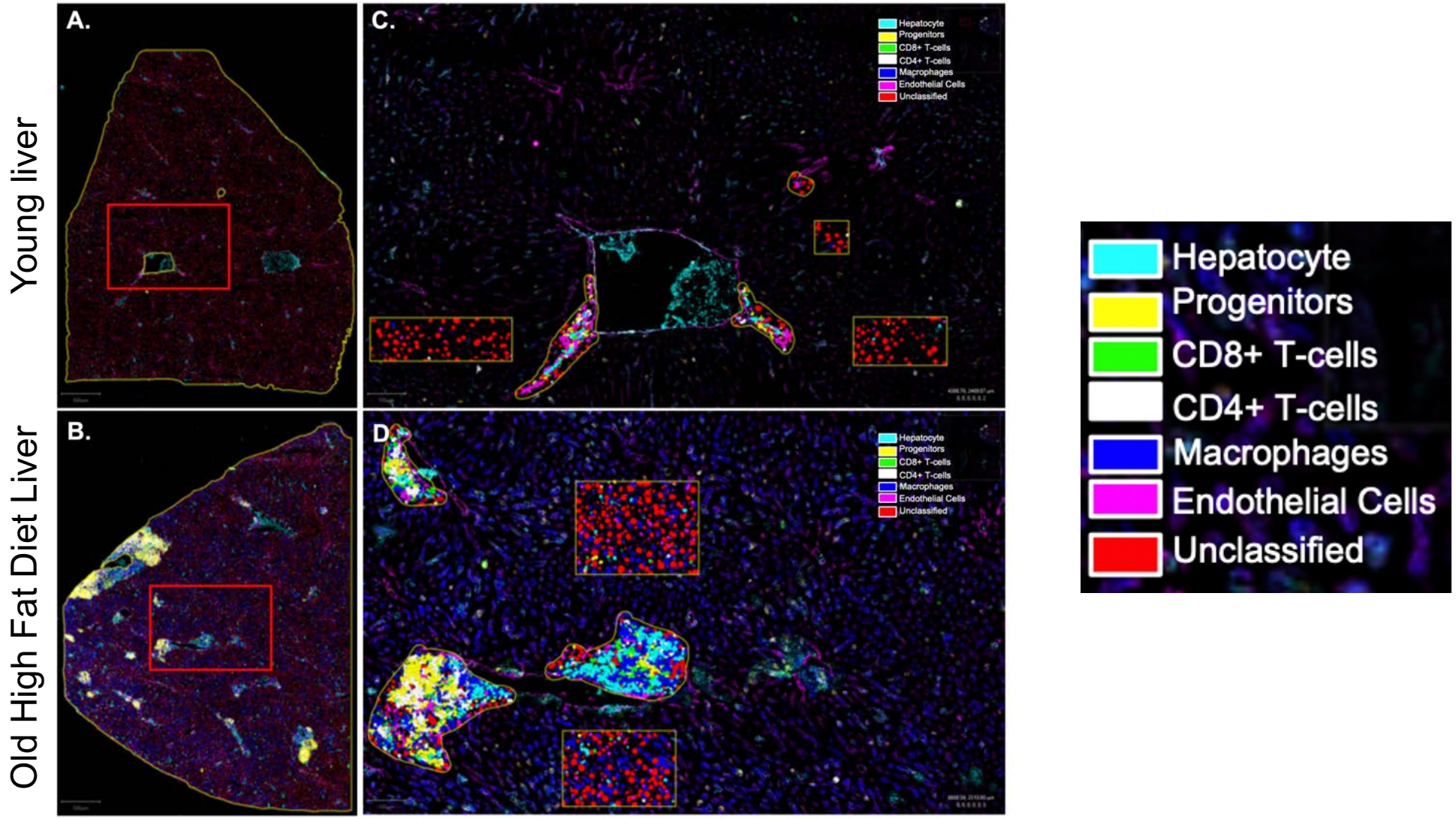


Cell – cell heterogeneity is a likely precursor to diseases of aging

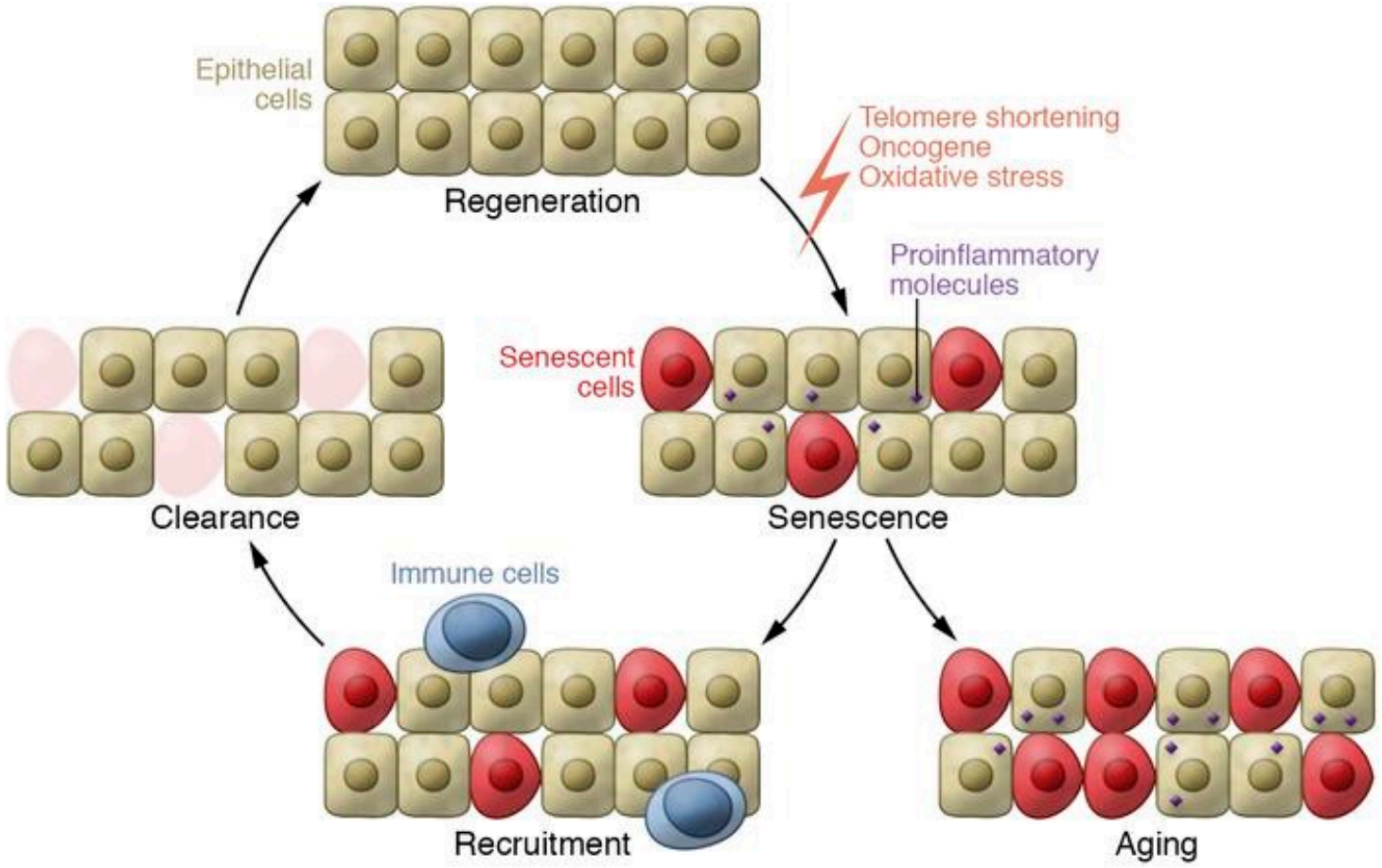
Function of young, healthy tissues depends on precise tissue organization and cell – cell interactions of multiple cell types.



Aged tissues show spatially restricted immune infiltration



Senescent cells accumulate in aged tissues



SenNet

New Funding Opportunities for the Cellular Senescence Network

RFA-RM-22-004 application deadline:1/18/22
RFA-RM-22-003 & 005 application deadline:1/19/22

Spatial –omics in San Diego

Nanostring GeoMx DSP

Salk
Sanford Burnham Prebys

Vizgen MERSCOPE

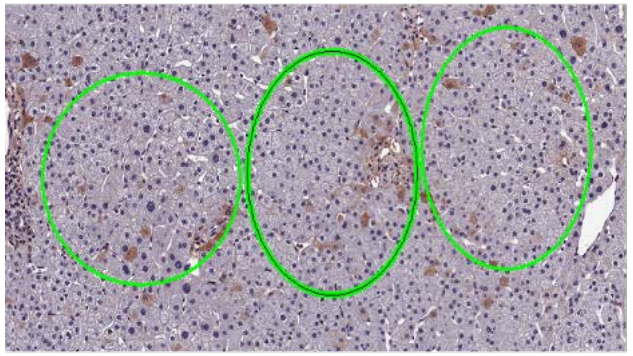
Salk
UCSD

Nanostring CosMx SMI

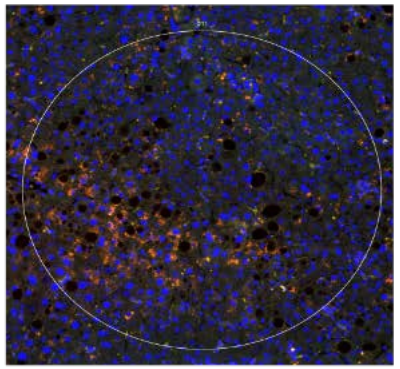
Sanford Burnham Prebys
(from June 2022)

Nanostring GeoMx to identify novel candidate ATF6 targets in liver disease

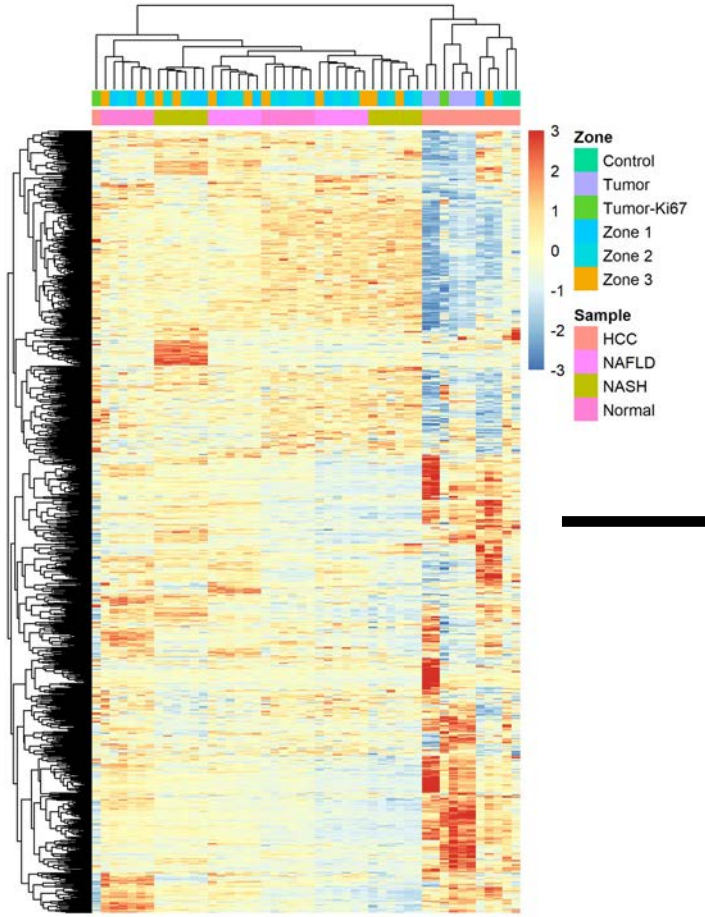
ATF6 IHC



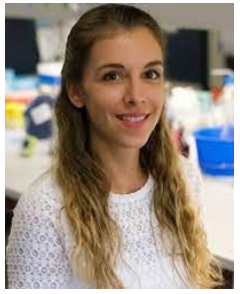
IF and ROI selection



1800 cancer atlas probes



Thbs1
Hsp90b1
targets of interest identified (among others)



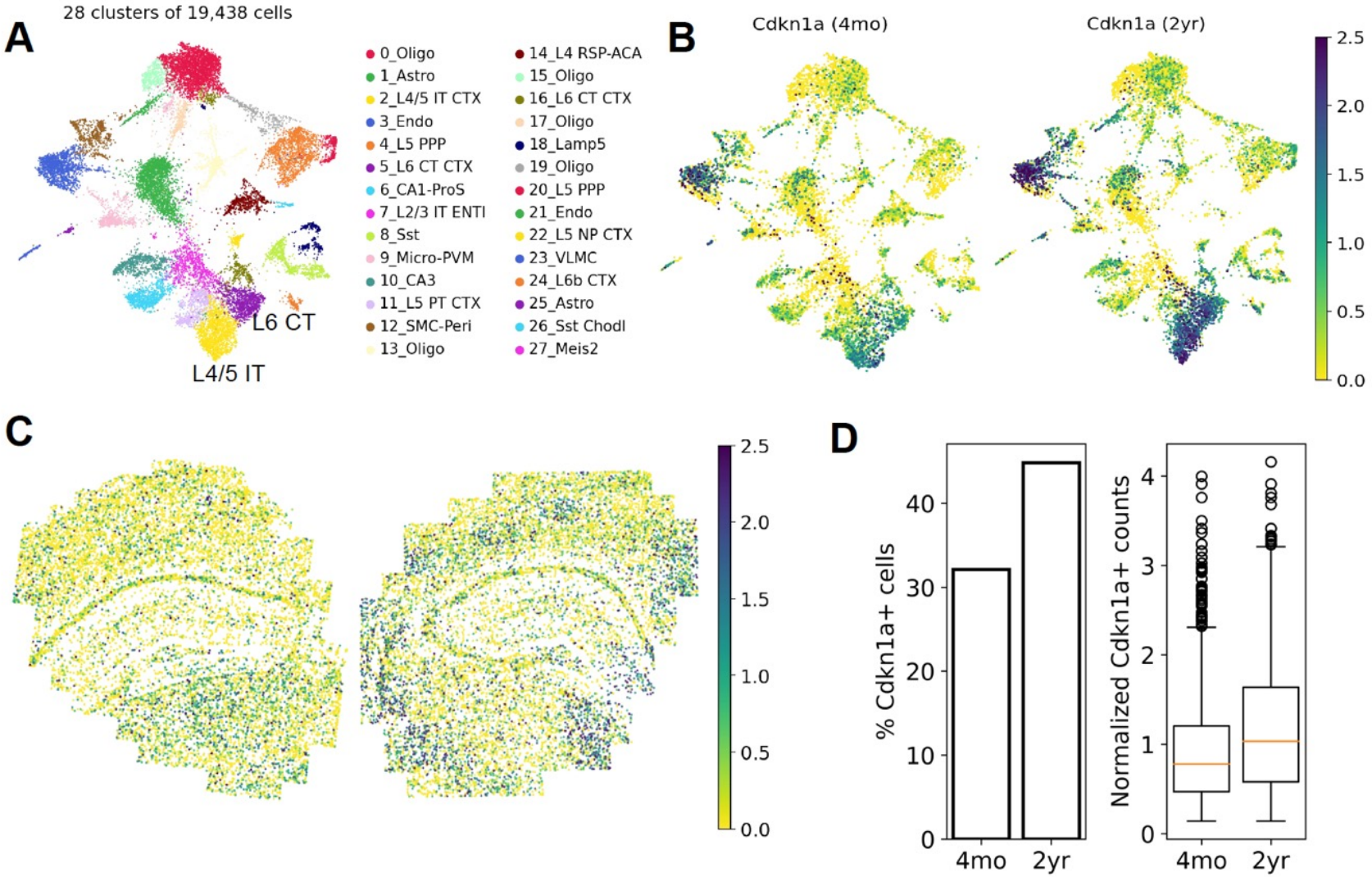
Cynthia Lebeaupin

Randy Kaufman

MERSCOPE to quantitate and map senescent cells in aged brain

Bing Ren

Quan Zhu



- URI MANOR: Age-related changes to cochlear hair cell organelle morphology
- JOLENE DIEDRICH: Mass Spectrometry
- NASUN HAH: Studying aging at single-cell resolution