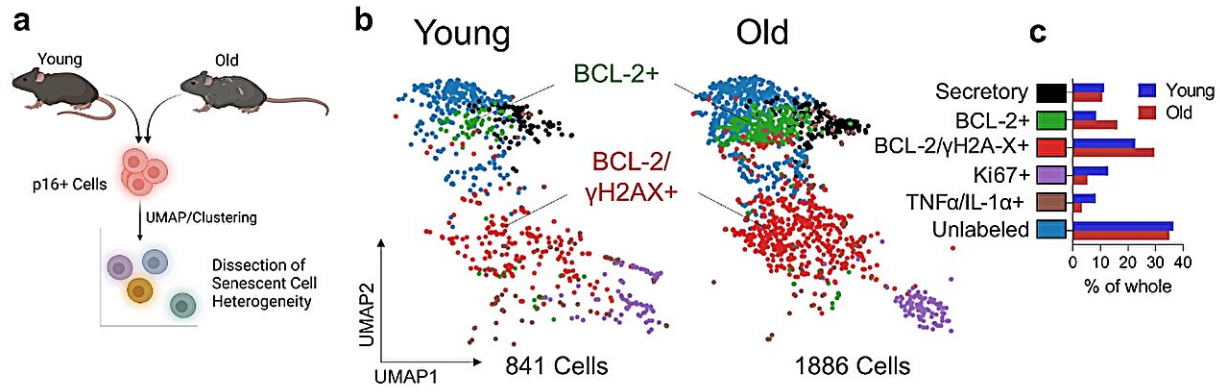
Zooming in on rare bone cells that drive osteoporosis

October 16 2023, by Caitlin Doran



BCL-2 expression defines p16+ cells with senescent characteristics. a Schematic of multidimensional p16+ senescent cell analysis workflow; b UMAP visualization and FlowSOM clustering of pooled p16+ cells from young (n = 15) and old (n = 12) mice with c bar graphs indicating percent-of-whole cluster abundance changes. Credit: *Nature Communications* (2023). DOI: 10.1038/s41467-023-40393-9

Mayo Clinic researchers have developed a new high-resolution, analytical technique to identify the rare senescent bone cells that are known to drive osteoporosis. Senescent cells are malfunctioning cells that build up as people age or as the result of chronic diseases. Once these cells form, they can contribute to developing diseases and consequences of aging.

This new method, detailed in a paper published in *Nature Communications*, will enable scientists to better target experimental anti-aging drugs at the cellular level, advancing efforts to find treatments for osteoporosis and other aging-related diseases.

"Senescent cells are notoriously challenging to identify. With this work, we are overcoming a barrier that has hindered past research," says Madison Doolittle, Ph.D., a Mayo Clinic endocrinology researcher and first author of the paper. "We expect this technique will enhance our ability to study these cells in a precise manner, understand the mechanisms of diseases and develop more focused targets for treatment."

This research will inform clinical trials at Mayo Clinic and around the world that are testing experimental treatments for osteoporosis, Alzheimer's disease, chronic kidney disease and other aging-related diseases. The new technique is already being used to map senescent cells through the National Institutes of Health's Cellular Senescence Network.

The new technique involves mass cytometry, a method scientists employ to analyze the differences among many types of cells and to identify specific cells by the types of proteins displayed on their surfaces or interiors. To pinpoint senescent cells, the researchers looked for the presence of p16, p21, BCL-2, and CD24 proteins, which control the development and survival of senescent cells.

"The novel, single-cell approach that Dr. Doolittle developed opens up new ways to identify these rare senescent cells not only in bone but also broadly across tissues," says Sundeep Khosla, M.D., a Mayo Clinic endocrinologist and senior author of the paper. "From a translational and clinical perspective, this would help in potentially quantifying the burden of senescent cells in patients and their response to interventions that kill or disable these harmful cells."

Dr. Khosla anticipates that future research will focus on applying this technique to identify strategies to improve bone healing and regeneration after skeletal injury.

More information: Madison L. Doolittle et al, Multiparametric senescent cell phenotyping reveals targets of senolytic therapy in the aged murine skeleton, *Nature Communications* (2023). DOI: 10.1038/s41467-023-40393-9

Provided by Mayo Clinic