

Immune System Profiles of Extremely Long-Lived People

The findings provide a basis for future studies of the immune system's role in longevity.

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The mix of various immune cells in the body changes with age. These changes may contribute to various age-related diseases. Many centenarians—people who live to at least 100 years—tend to have delayed onset of age-related diseases such as cancer, stroke, and cardiovascular disease. This suggests that their immune systems remain healthier for longer compared with other people.

A previous study in Japan did an analysis of immune cell gene expression patterns—when genes are turned on and off—and found that immune cell composition in centenarians differed from that in younger people. It isn't clear if these results generalize to other ethnicities. The gene expression changes of individual immune cell types with age also weren't closely studied.

An NIH-funded team, led by researchers at Boston University and Tufts Medical Center, sought to address these questions. To do so, they performed single-cell RNA sequencing (scRNA-seq) of more than 16,000 immune cells. The cells came from seven centenarians and, for comparison, two people in their 30s and 40s. The researchers also classified the various cells based on 10 cell-surface proteins. They then combined their data with publicly available scRNA-seq datasets. This yielded a total sample of more than 102,000 cells from 66 people.

The team divided the people into four age groups: 12 of younger age (20–39 years), 26 of middle age (40–59 years), 14 of older age (60–89 years), and 14 centenarians. The results appeared in the [April 2023 issue of eBioMedicine](#).

The researchers observed a decreased ratio of lymphocytes (a type of white blood cell that includes T cells and B cells) to myeloid cells (part of the innate immune system, including monocytes and dendritic cells) with age. This was an expected change with aging. Among the lymphocytes, centenarians had more B cells (which produce antibodies) and fewer T helper cells (which help coordinate other immune cells) compared with younger people. This change was unique to centenarians and did not occur in older non-centenarians.

These shifts, taken together, suggest that, over their lifetimes, the centenarians developed faster, more effective immune responses to infections. For example, B cells respond faster to infections than T cells.

The team found 35 genes whose expression changed in immune cells with age, including genes involved in repairing DNA damage. Another 25 genes appeared to be expressed only in centenarians. This included the gene S100A4, which has been implicated in aging-related diseases and longevity. The gene expression changes in centenarians also suggest changes in general metabolic regulation.

The results suggest specific immune adaptations that may contribute to centenarians' extreme longevity. "Our data support the hypothesis that centenarians have protective factors that enable them to recover from disease and reach extreme old ages," says lead author Dr. Tanya Karagiannis of Tufts.

Given the small number of centenarians studied, these results should be considered preliminary. The findings also can't reveal whether the observed changes may be causes or consequences of living a long life. Even so, they provide a foundation for further exploring the role of immune resilience in longevity.

This [research summary](#) was published by the National Institutes of Health on April 25, 2023.