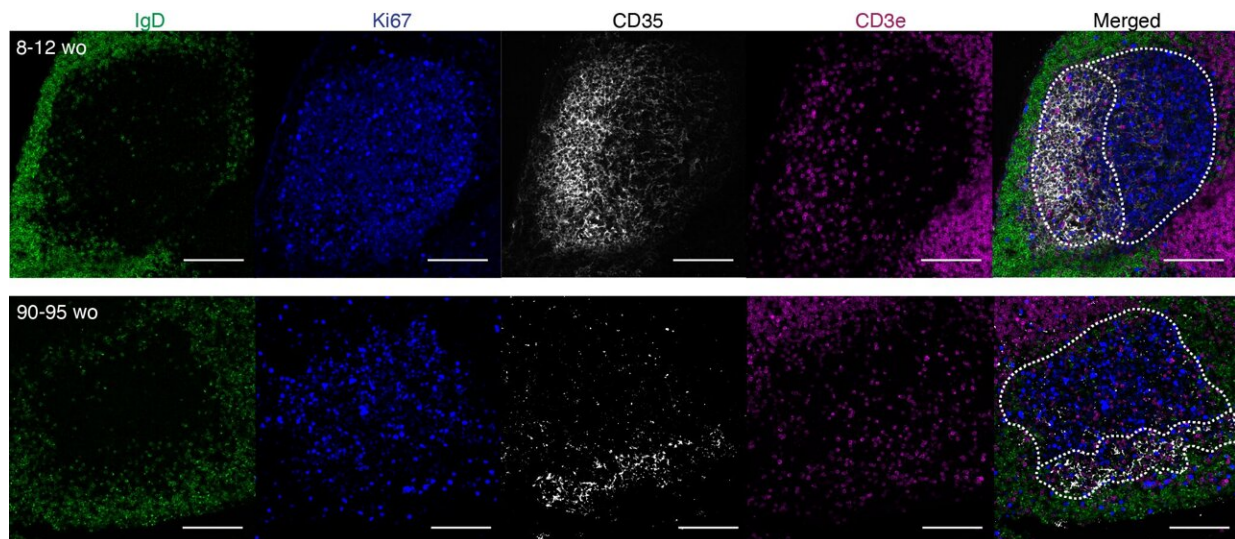


'Lost' immune cells partly to blame for reduced vaccine response in older people

May 22 2023



Microscopy image of a germinal center structure which is altered in aged mice.
Credit: Babraham Institute

Understanding the ways our immune response changes as we age holds the key to designing better vaccines and boosting protection for people most at risk. Research published by Dr. Michelle Linterman and her group today in *Nature Immunology* has explained that the organization of the germinal center, which is vital to the generation of longer-lived protection following vaccination, is altered in aging.

By demonstrating that these age-related changes can be reversed in mice,

the research sets the foundation for interventions that bolster an effective vaccine response.

After a vaccination our immune system reacts by creating specialized structures called germinal centers that produce the [immune cells](#) (B [cells](#)) that provide long-term protection through the production of antibodies. Due to an age-dependent impairment in antibody production, [older people](#) have lower levels of protection from vaccination which also wanes more quickly compared to younger people. Protection by vaccination is essential to protect older people who become more susceptible to infections with age.

Therefore, understanding how the age-related decline of the [immune system](#) can be reversed or mitigated is an important part of securing better health in later years.

The correct function of the germinal center response requires the coordination of cellular interactions across time and space. Germinal centers are made up of two distinct regions—the light zone and dark zone, with some cells located in specific areas, and others which move between the zones. B cells are shaped by their interactions in first the dark zone and then in the light zone.

Through a combination of mouse research, computer modeling and analysis of human vaccination data, the Linterman lab research team were able to show that changes to key interactors of B cells in the light zone of the germinal center, T follicular helper cells, and also to light-zone specific cells called follicular dendritic cells (FDCs), were at the heart of the diminished vaccination response.

Dr. Michelle Linterman, a group leader in the Institute's Immunology program, explains "In this study we looked at what was happening to different cell types in the germinal center, particularly the structure and

organization of the germinal center across its two functionally distinct zones, to try and understand what causes the reduced germinal center response with age."

"What we found is that the T follicular helper cells aren't where they should be and as a result, antibody-producing cells lose essential selection cues. Surprisingly we also uncovered an unknown role for T follicular helper cells in supporting the expansion of follicular dendritic cells in the light zone after vaccination."

The team used 3D computer modeling to simulate the loss of Tfh cells from the light zone and a reduced FDC network, which recapitulate their findings and strengthened their hypothesis that these two factors were enough to be responsible for a suboptimal germinal center response in aged mice.

Having identified the dependencies between the [cell types](#), the researchers used genetically modified mice to control the location of Tfh cells in the germinal center, demonstrating that the defective FDC response was caused by loss of Tfh from the light zone. Importantly, they were also able to correct the defective FDC response and boost the germinal center response in aged mice by providing T cells that could correctly localize to the light zone.

The team also utilized data from human vaccination studies and found similar age-dependent changes in mice and humans.

"These findings give us a more complete picture of what the effects of age are on the germinal center and vital insight into how we might address these in terms of developing effective strategies for enhancing [vaccine](#) response in older people," concludes Dr. Linterman.

More information: Michelle Linterman, Spatial dysregulation of T

follicular helper cells impairs vaccine responses in aging, *Nature Immunology* (2023). DOI: [10.1038/s41590-023-01519-9](https://doi.org/10.1038/s41590-023-01519-9).
www.nature.com/articles/s41590-023-01519-9

Provided by Babraham Institute

Citation: 'Lost' immune cells partly to blame for reduced vaccine response in older people (2023, May 22) retrieved 5 May 2024 from
<https://medicalxpress.com/news/2023-05-lost-immune-cells-blame-vaccine.html>

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