

# Relative Deficiency in Interferon- $\gamma$ -Secreting CD4+ T Cells is Strongly Associated with Poorer COVID-19 Vaccination Responses in Older Adults\*

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## BACKGROUND

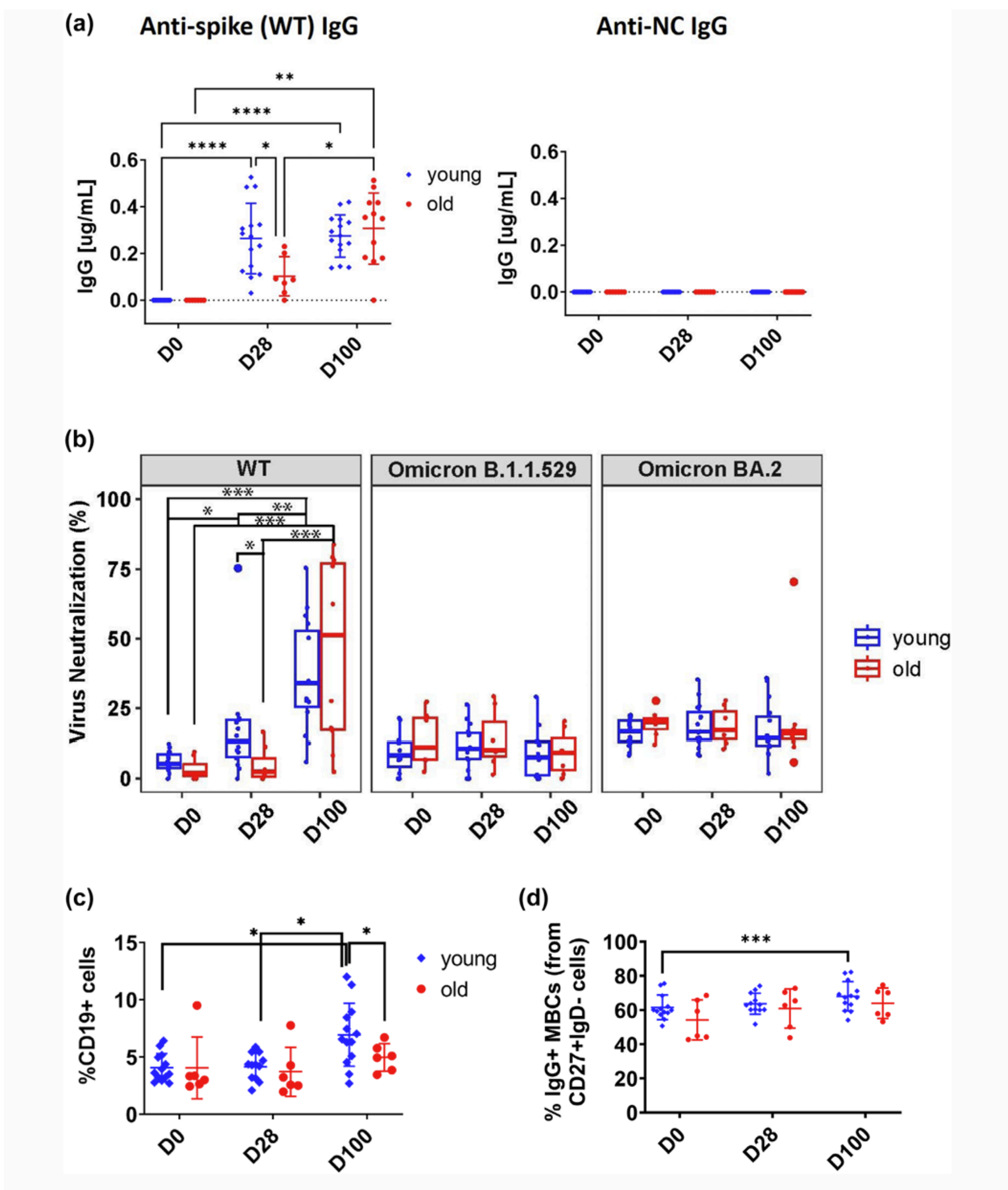
Older adults have poorer COVID-19 vaccination outcomes due to immunosenescence and inflammaging, which impair T-cell function and antibody responses. While COVID-19 mRNA vaccines are effective, their efficacy is significantly reduced in this age group. Previous research shows diminished cytokine production and weaker immune responses in older adults, but the role of IFN $\gamma$ -secreting CD4+ T-helper cells is not fully understood.

This study investigates how age affects these T cells to clarify reduced vaccine efficacy in older adults.

## HYPOTHESIS

The relative deficiency of IFN $\gamma$ -secreting CD4+ T cells in older adults contributes to weaker COVID-19 vaccine-induced immune responses compared to younger adults.

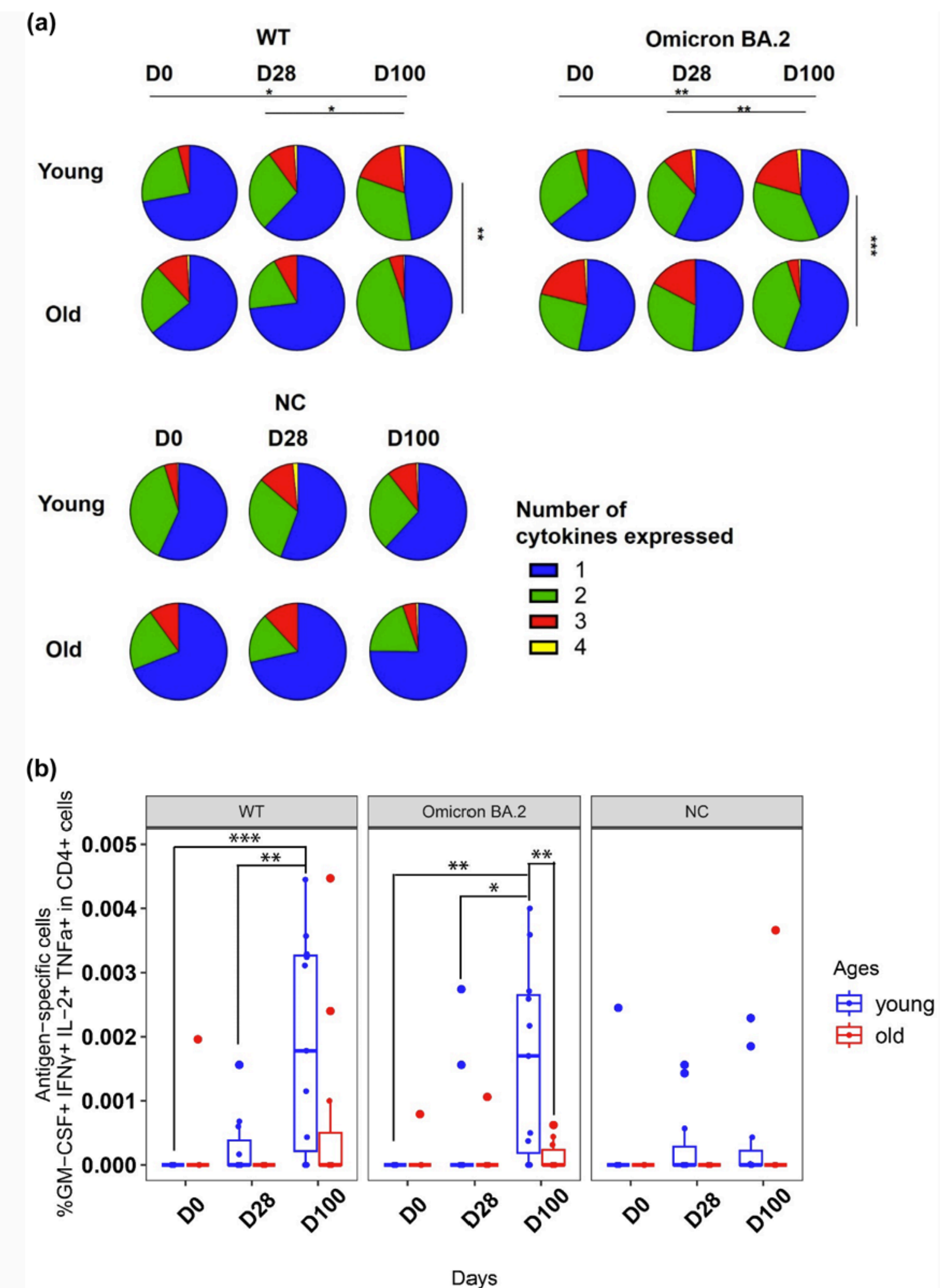
## RESULTS



## METHODOLOGY

The study analyzed immune responses in 29 community-dwelling adults (15 young, median age 31; 14 older, median age 72) after two doses of the BNT162b2 vaccine. Blood samples were collected at baseline, 28 days post-first dose, and 100 days post-second dose. Researchers assessed neutralizing antibody levels, B-cell subsets, and antigen-specific T-cell responses using ACE-2 inhibition assays, flow cytometry, and intracellular cytokine staining.

The focus was on IFN $\gamma$ -secreting CD4+ T cells and their correlation with neutralizing antibody responses to identify age-related differences in vaccine efficacy.



- Younger adults demonstrated higher neutralizing antibody responses to SARS-CoV-2 wild-type and variants compared to older adults. While older participants exhibited increases in neutralizing antibodies after vaccination, the changes were less pronounced and often non-significant.
- B-Cell Responses: Vaccination induced a significant expansion of IgG+ memory B cells in younger adults, but this response was diminished in older adults. Both groups showed a reduction in IgA+ memory B cells post-vaccination.
- CD4+ T-Cell Responses: Younger adults showed a robust increase in IFN $\gamma$ -secreting CD4+ T cells and polyfunctional CD4+ T cells (producing multiple cytokines) after vaccination. In older adults, these T-cell responses were weaker or absent.
- Correlation with Antibody Responses: IFN $\gamma$ -secreting CD4+ T cells positively correlated with neutralizing antibody levels in younger adults, a relationship not observed in older adults.
- CD8+ T-Cell Responses: Older adults displayed higher levels of senescent CD8+ T cells (TEMRA cells) and fewer naïve CD8+ T cells, which may contribute to their diminished immune responses.

## CONCLUSION

The study found that older adults had weaker COVID-19 vaccine responses, with lower antibody levels, impaired B-cell development, and fewer IFN $\gamma$ -secreting CD4+ T cells. In younger adults, these T cells correlated with stronger antibody responses, but not in older adults. These findings suggest the need for tailored vaccination strategies for aging populations.

\*Ho, V. W. T., Boon, L. H., Cui, J., Juequn, Z., Shunmuganathan, B., Gupta, R., Tan, N. Y. J., Qian, X., Purushotorman, K., & others. (2024). Relative deficiency in interferon- $\gamma$ -secreting CD4+ T cells is strongly associated with poorer COVID-19 vaccination responses in older adults. *Aging Cell*, 23(4), e1409.