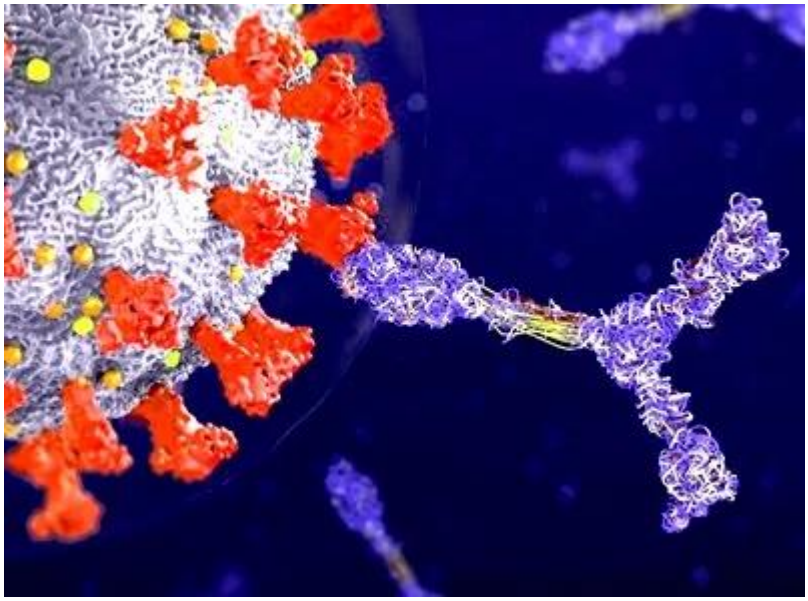
After vaccination with messenger RNA (mRNA)-based BNT162b2 vaccines (Corminaty, BioNTech/Pizer), humoral immune responses are predominantly composed of immunoglobulin (Ig) G1 and IgG3 subclass antibodies, which are capable of mediating effector functions such as antibody-dependent cytotoxicity, phagocytosis, and complement activation. Irrgang et al were the first to report an increased proportion of SARS-CoV-2 spike (S) protein–specific IgG4 in adults, starting after the second and increasing further after the third mRNA vaccine dose. https://discovermednews.com/repeated-sars-cov-2-mrna-vaccination-results-in-a-class-switch-to-noninflammatory-spike-specific-igg4-antibodies/ In this article the authors from Germany measured SARS-CoV-2 spike subunit 1 (S1)–specific and receptor-binding domain (RBD)-specific IgG subclasses to investigate the induction of IgG4 following BNT162b2 vaccination in children 5-11 years of age. This study reported, for the first time in children, significantly elevated levels of IgG4 antibodies specific for the SARS-CoV-2 S1 and RBD one year after the second mRNA BNT162b2 vaccination compared to baseline.



After the second and third mRNA vaccination, Irrgang observed not only an increased proportion of S protein-specific IgG4 in adults but also a reduced ability of antibodies specific to the S protein to mediate antibody-dependent cellular phagocytosis and complement deposition. Importantly, IgG4 levels increased from 0.04% shortly after the second vaccination to 19.27% late after the third vaccination. The levels of all other IgG subclasses decreased during the same period.

SARS-CoV-2 is an enveloped, positive-sense, single-stranded RNA virus. Its genome encodes four structural proteins, namely the spike (S), envelope (E), nucleocapsid (N), and

membrane (M) protein. The S protein is composed of subunits S1 and S2, separated by host cell proteases. The S1 domain comprises the N-terminal domain (NTD), the receptor binding domain (RBD) with a receptor binding motif (RBM), and two C-terminal domains. The RBD in the S1 subunit recognizes human ACE2 and is responsible for attachment to host cells.

About the study

The authors used a bead-based multiplex immunoassay to determine the induction of IgG4 after BNT162b2 vaccination in 14 healthy children, 5-11 years of age (median age 8.5 years). The study included 6 girls and 8 boys.

The children were vaccinated with two doses of BNT162b2 (10 µg) with a median interval of 27.5 days between doses. Blood was collected on the day of the first dose, five weeks, and one year after the second dose.

All participants experienced mild postvaccination reactions. Previous SARS-CoV-2 infection was confirmed in 2 children with a history of mild COVID-19. Upon the emergence of the Omicron variant, all children were infected with no or only mild symptoms by the time of long-term follow-up and showed positive hybrid immunity responses.

Results

Five weeks after the second BNT162b2 vaccination, the children's antibody response was dominated by the IgG1 and IgG3 subclasses, which decreased over time. The levels of IgG2 and IgG4 were relatively low.

One year after the second BNT162b2 vaccination, the levels of IgG4 antibodies specific for S1 and RBD significantly increased compared to baseline. Infection-naive children at the time of first vaccination had higher IgG4 levels than previously infected individuals.

According to the authors, it is unclear how delayed IgG2 and IgG4 induction by mRNA vaccination affects long-term immunity. IgG4, as the least abundant IgG subclass in humans, has some unique structural and functional features that lead to it being described as a "blocking" and "anti-inflammatory" antibody that cannot activate antibody-dependent immune effector responses. One possible explanation is related to the role of CD4+ T follicular helper cells in establishing long-term immunity elicited by this new type of vaccine and the pathogenesis of IgG4-related diseases.
https://discovermednews.com/two-case-reports-of-igg4-related-disease-after-anti-sars-cov-2-

vaccination/

Conclusion

In this study, as previously described in adults, an increase in IgG4 levels specific for S1 and RBD was observed in children one year after BNT162b2 vaccination. The authors concluded that more attention should be paid to IgG4 responses as more mRNA vaccines are being developed. They hope these findings will stimulate further research into the similarities and differences in the immune responses of adults and children, particularly concerning the switching of IgG subclasses and the functionality of vaccine-induced antibodies.

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