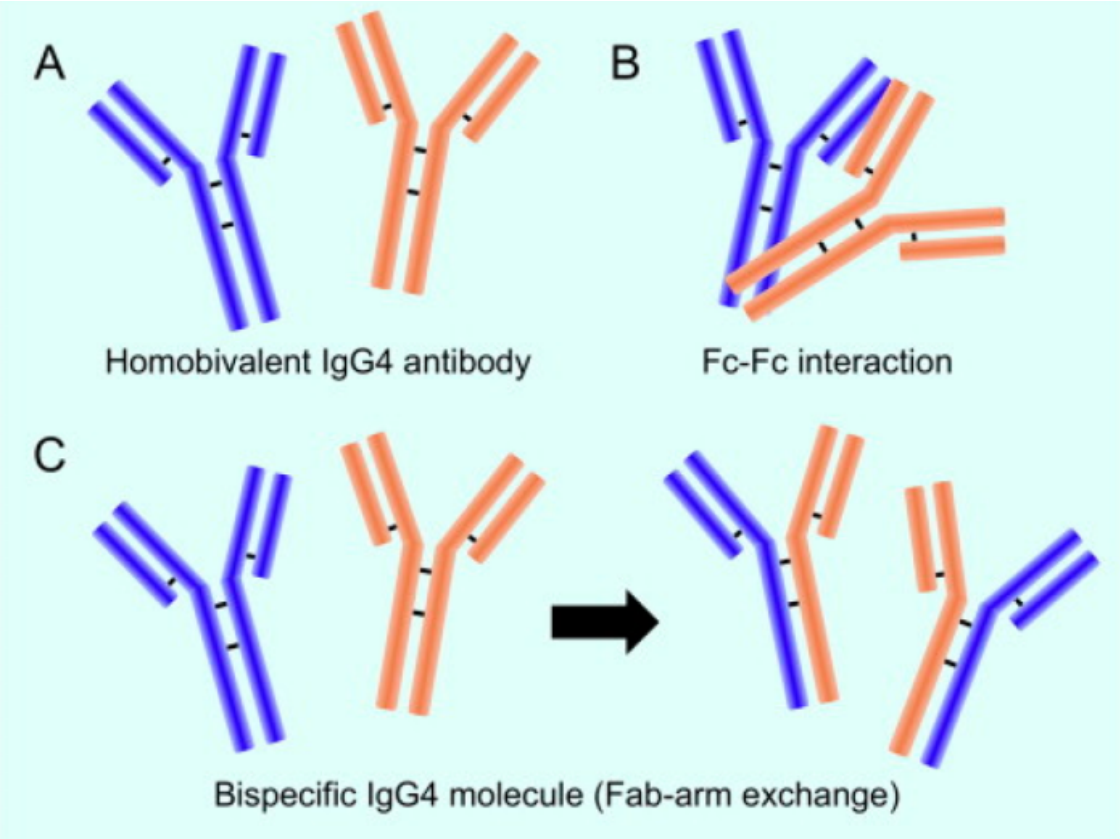
IgG4 Increases with Repeated mRNA Vaccines: Linked to Disease

By **Wendi Strauch Mahoney** - May 30, 2023



IgG4 /https://www.mdpi.com/2076-393X/11/5/991

A peer-reviewed study entitled "IgG4 Antibodies Induced by Repeated Vaccination May Generate Immune Tolerance to the SARS-CoV-2 Spike Protein" reports, "recent investigations have found abnormally high levels of IgG4 in people who were administered two or more injections of the mRNA vaccines." The paper states, "compelling evidence shows that among COVID-19 vaccines, only the mRNA vaccines (but not the adenoviral vector-based vaccine from AstraZeneca) induced a remarkable increase in IgG4 levels."

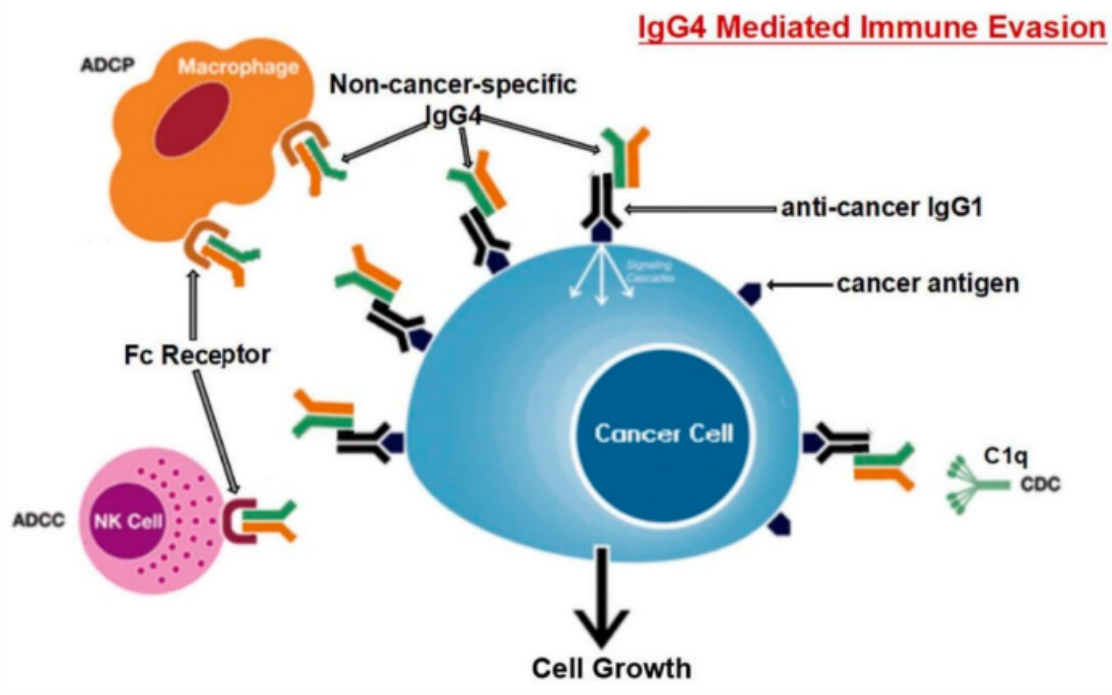
The paper was published on May 17, 2023, in a special issue entitled "SARS-CoV-2: Immune Tolerance and Autoimmune Diseases after COVID-19 Vaccination and Its Related Adverse Events" of the Vaccines Journal featured in the "COVID-19 Vaccines and Vaccination" section of the Journal featuring 1397 papers on all facets of the COVID-19 vaccines and their administration.

Dr. Mikolaj Raszek, Founder and managing director of Merogenomics Inc., provides an excellent summary explanation of the findings below:

Repeated Doses of mRNA Vaccines Increase IgG4 Levels

The paper's findings are worrisome because it shows evidence that repeated mRNA vaccinations can cause disease due to increased IgG4 levels. According to the paper, "Increased IgG4 synthesis due to repeated mRNA vaccination with high antigen concentrations may also cause autoimmune diseases and promote cancer growth and autoimmune myocarditis in susceptible individuals."

Figure 3. The suggested pathway for immune evasion evolved by cancer cells through IgG4 produced from B lymphocytes is depicted diagrammatically. Prolonged exposure to cancer antigens causes B cells to change their class and generate IgG4. With its Fc-Fc binding characteristic, such enhanced IgG4 can interact with cancer-bound IgG as well as Fc receptors on immune effector cells. Increased IgG4 in the cancer microenvironment promotes an efficient immune evasion mechanism for cancer due to its special structural and biological properties. The acronyms ADCC, ADCP, CDC, and NK stand for antibody-dependent cell-mediated cytotoxicity, antibody-dependent cell phagocytosis, complement-dependent cytotoxicity, and natural killer cells, respectively. Reproduced from [101]. This is an open-access article distributed under the Creative Commons Attribution Non-Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial.



IgG4 Immune Evasion/Figure 3/https://www.mdpi.com/2076-393X/11/5/991

Importantly, the paper also notes that "lethal COVID-19 cases have been linked to higher levels of IgG4 antibodies, and it has also been documented that mRNA vaccines trigger their synthesis." Researchers have thus begun to look at the effect of repeated doses of the

The paper confirms what is becoming increasingly apparent to anyone who has been paying attention—immunity from mRNA vaccines "rapidly wanes." The paper also confirms that mRNA vaccines do not prevent hospitalization and severe disease in people with comorbidities and that the vaccines "do not produce sterilizing immunity." As a result, many individuals "suffer frequent re-infections" of the virus. According to the paper, "All three anti-COVID-19 vaccines: Pfizer, Moderna, and Astra Zeneca ChAdOx1, (Cambridge, UK) appeared to be only transiently protective against SARS-CoV-2 infection and transmission."

Increase in IgG4 Levels Suppress "Natural Antiviral Responses"

Researchers found that IgG4 levels increased with repeated vaccinations, causing a breakdown in "natural antiviral responses," promoting illness and disease. According to the paper, "the reported increase in IgG4 levels detected after repeated vaccination with the mRNA vaccines may not be a protective mechanism."

IgG4 is the least common subclass of IgG (a subclass of antibodies). According to dermnetnz.org, "IgG accounts for 75% of antibodies circulating in the blood, which are an essential part of the secondary immune response to infection and toxins." It was initially thought that an increase in IgG4 could have a protective role, according to the study. In fact, researchers are seeing the opposite.

> *"Overall, there are three critical factors determining the class switch to IgG4 antibodies: excessive antigen concentration, repeated vaccination, and the type of vaccine used. It has been suggested that an increase in IgG4 levels could have a protecting role by preventing immune over-activation, similar to that occurring during successful allergen-specific immunotherapy by inhibiting IgE-induced effects. However, emerging evidence suggests that the reported increase in IgG4 levels detected after repeated vaccination with the mRNA vaccines may not be a protective mechanism; rather, it constitutes an immune tolerance mechanism to the spike protein that could promote unopposed SARS-CoV2 infection and replication by suppressing natural antiviral responses."*

Vaccinated v. Unvaccinated: U.S. and U.K. Show Conflicting Data on Mortality Rates

The study also points out some important conflicting information on mortality rates. The CDC has reported throughout the pandemic that "mortality rates have been higher in the unvaccinated than the vaccinated." However, the UK's Office for National Statistics (ONS) begs to differ. Initially, data collected between April to Mid-November 2021 seemed to show that mortality was higher in the unvaccinated. But later data collected from the end of November 2021 to December 2022 showed a reversal in the data, showing higher death rates in the repeatedly vaccinated or those who took the third dose.

Additionally, investigations of vaccination uptake in Europe, beginning in 2021 through

All-cause mortality during the first 9 months of 2022 increased more in countries with higher 2021 vaccination uptake, according to analyses of 31 countries estimated by population size; a one percentage point increase in 2021 vaccination uptake was associated with a monthly mortality increase in 2022 of 0.105% (95% CI, 0.075–0.134). The relationship remained strong after adjusting for alternative factors."

IgG4-related disease (IgG4-RD) seems to produce a disease that is "autoimmune in origin" and inflammatory in nature. The paper states, *"IgG4-RD includes a "wide variety of diseases, formerly diagnosed as Mikulicz's disease (MD) [66], autoimmune pancreatitis (AIP) [67], Riedel thyroiditis [68], interstitial pneumonitis [69,70], interstitial nephritis [71,72], prostatitis, lymphadenopathy [73,74], retroperitoneal fibrosis (RPF) [75,76], and inflammatory aortic aneurysm [77]". It also plays a significant role in the pathogenesis of at least 13 autoimmune disorders. It has been shown that laboratory animals passively infused with human total IgG or IgG4 develop signs in 5 of these 13 disorders, proving the pathogenicity of this antibody."*

mRNA vaccines are not the only vaccines that induce IgG4 antibody production. The paper states, "The HIV, Malaria, and Pertussis vaccines also elicited such a response. Overall, there are three critical factors determining the class switch to IgG4 antibodies: excessive antigen concentration, repeated vaccination, and the type of vaccine used."

"Dose Escalation" May Cause Numerous Negative Responses

The paper quotes "major findings" concerning administering repeated doses of a given vaccine. While "dose escalation" may prove necessary for clinical phase 1 vaccine investigations "to find a dose that produces the best response," there are well-investigated arguments against that kind of protocol for later investigations and public administration. Repeated doses can cause cell death, immune tolerance, "terminal differentiation of T-cells," adverse symptoms with additional dosing, and "immune exhaustion."

(1) When excessive quantities of antigen are injected, it can cause cell death, resulting in the loss of a specific group of T cells; this phenomenon is known as clonal deletion.

(2) Immune tolerance may develop as a result of prolonged antigen exposure. T cells are an essential part of the immune system that detects and removes infections and other foreign objects. Yet, these T cells may become desensitized and lose their capacity to react to repeated exposures when they are exposed to large concentrations of antigens, such as during repeated vaccination. Immune tolerance is a condition that can also result in the persistence of infections or the emergence of autoimmune diseases.

(3) T cells can undergo a process known as "terminal differentiation" when vaccines are given in high concentrations, at which point they become highly specialized, losing the capacity to divide and proliferate. The immune system becomes exhausted as a result and is unable to mount a successful defense against subsequent illnesses. This is a problem since it might undermine the protective advantages of vaccinations. To balance the advantages of immunological protection and the potential disadvantages of immune exhaustion, it is crucial to carefully determine the ideal dose of vaccines.

(4) Adverse outcomes are more likely to occur in groups receiving greater doses.

(5) The intensity of the reaction between an antigen and a T cell receptor or an antibody is referred to as avidity. The immune response is more effective in identifying and removing the target antigen when avidity is high. High antigen dosages, however, can result in "immune exhaustion," a condition where the immune system's cells become desensitized and unable to mount a successful defense. Helper T cell and antibody avidity may decline as a consequence, impairing the immunological response to the target antigen. To establish a strong and effective immune response, it is crucial to thoroughly assess the ideal antigen dosages utilized in immunotherapy [108].

Billeskov et al. [108] provided proof of cases where lower vaccine antigen doses resulted in more positive responses from T cells, both for quality as judged by several effector capabilities and preventive efficiency in both animal and human experiments, and they presented arguments for the significance of reducing antigen dose for optimum protection in some models. They also encouraged experts in T-cell vaccination, in particular, to remember that sometimes, less certainly is more. In conclusion, is there a link between antigen dose concentration, repeated exposure, and the induction of IgG4 production? Or is the elevated IgG4 concentration associated with COVID-19 vaccination due to genetic predisposition? Because approximately half of the vaccinees showed a substantial increase in IgG4 concentration after the second mRNA inoculation [30], it is evident that such an increase is not caused by a genetic predisposition. Moreover, Moderna and Pfizer used the same antigen dose for their primary and booster vaccinations, which contradicts the vaccinology paradigm showing that a low antigen dose is recommended for boosting [110,111].

Repeated Doses/Arguments Against/IgG4 Antibodies Induced by Repeated Vaccination May Generate Immune Tolerance to the SARS-CoV-2 Spike Protein

The paper concludes that negative outcomes from mRNA vaccines "are not expected to affect all people who have received the mRNA vaccines." They posit that individuals may be more susceptible to negative outcomes if they suffer from "genetic susceptibility, immune deficiencies, and comorbidities." However, these vulnerabilities highlight an important observation noted by those who wrote the paper:

> *"[I]f people who are the most affected by the COVID-19 disease (the elderly, diabetics, hypertensive, and immunocompromised people like those with HIV) are also more susceptible to suffering the negative effects of repeated mRNA vaccination, is it then justified to booster them? As Omicron subvariants have been demonstrated to be less pathogenic and mRNA vaccines do not protect against re-infection, clinicians should be aware of the possible detrimental effects on the immune system by administering boosters."*

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