Covid-19 mRNA Injections and links to Cancer development

Introduction

The aim of this article is to demonstrate the need for further investigation into the link between Covid-19 mRNA injections and the recent rise in cancer cases Worldwide.

It has been observed by many in the medical research community that repeated Covid-19 mRNA injections produce large quantities of an antibody called igG4 (immunoglobulin G4) which subsequently turns off the human body's ability to identify and destroy cancer cells and other severe disease.

The development of this large quantity of igG4 is usually around the third Covid-19 mRNA injection according to the literature and occurs via a mechanism called class switching where antibodies igG1 and igG3 convert to igG4 and igG2 after a period following inoculation.

There are 4 subclasses of igG antibodies with 1 and 3 being the ones with the highest potential to activate a positive immune response, and 2 and 4 not being so favourable. Numbers 1 and 3 are generated initially after receiving a Covid-19 mRNA injection. Preliminary test results from the Covid-19 mRNA injections will appear promising for fighting infection due to 1 and 3 but because of the class switching to 4 and 2 this quickly diminishes and breakthrough infections will become prevalent and little to no protection will be given. Also immune responses will be deactivated leaving individuals more susceptible to disease than prior to the mRNA treatment due to the inhibitor action of igG4 on Natural Killer Cells and igG1 and igG3 antibodies.

There is only a relatively small amount of research on this particular subject but what has been conducted clearly proves that further investigations are urgently needed, and a reevaluation of the requirement that these injections be offered to people as a beneficial therapeutic by our healthcare services.

Below is a collection of published medical journal excerpts which establish a decent foundation for this hypothesis and a clear urgency to push this issue forward for a comprehensive inquest.

Post-vaccination IgG4 and IgG2 class switch associates with increased risk of SARS-CoV-2 infections

https://www.sciencedirect.com/science/article/pii/S0163445325000672

Repeated COVID-19 mRNA vaccinations increase SARS-CoV-2 IgG4 antibodies, indicating extensive IgG class switching following the first booster dose. This shift in IgG subclasses raises concerns due to the limited ability of IgG4 to mediate Fc-dependent effector functions.

Here, we show that higher levels of IgG4 and IgG2, as well as higher proportions of non-cytophilic to cytophilic antibodies, following booster vaccination, are associated with a heightened risk of SARS-CoV-2 breakthrough infection. Conversely, IgG1 levels, C1q- and Fcγ receptor-binding antibodies and neutralization capacity are associated with protection.

Our study aligns with previous research showing a sharp increase in IgG4 and IgG2 levels following three doses of mRNA vaccination against SARS-CoV-2,1, 2 but goes beyond the state-of-the-art by ***associating this switch with decreased neutralization, Fc-effector functionality, and protective immunity.***

Nevertheless, while our findings indicate that higher IgG4 and IgG2 levels are associated with an increased risk of SARS-CoV-2 breakthrough infection, these less immune-activating subclasses may also help prevent severe COVID-19 by mitigating inflammation-driven pathology.[20] *Previous studies have also reported negative correlations between Fc-effector functions and IgG4 induction. For instance, ADCP phagocytosis scores and ADCD were reduced after the third mRNA vaccine dose compared to the second dose, with these reductions correlating with increased anti-S IgG4 levels.*[1] *Similarly,* ***a higher anti-S IgG4/IgG1 ratio after SARS-CoV-2 mRNA vaccination was associated with diminished NK (Natural Killer) cell activation and ADCD.***[6] *Beyond its reduced ability to engage effector functions, IgG4 is functionally monovalent due to its capacity for Fab-arm exchange,*[21] *which may limit its ability to form immune complexes and effectively neutralize pathogens.*

(From Google: Natural killer (NK) cells, a type of white blood cell, are crucial for the body's innate immune system, playing a vital role in detecting and eliminating virus-infected and cancerous cells, as well as regulating other immune responses.)

Both IgG2 and IgG4 B-cells typically accumulate high levels of somatic hypermutations, indicative of extensive affinity maturation. This suggests that antibodies of these subclasses may exhibit high binding affinities for their target antigens, which is generally important for neutralization. ***However, despite this potential for high affinity, we observed a negative association between IgG2 and IgG4 levels and neutralizing antibody responses.***

The underlying mechanisms driving class-switch recombination towards IgG4, especially after repeated COVID-19 mRNA vaccination, are still unclear. It has been hypothesized that persistent germinal centre responses induced by mRNA vaccination[22]*—possibly driven by the prolonged presence of vaccine mRNA or antigen in lymph nodes*[23]*—may facilitate class switching toward distal subclasses such as IgG4.*[2]

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

https://pmc.ncbi.nlm.nih.gov/articles/PMC10222767/

Additionally, recent investigations have found abnormally high levels of IgG4 in people who were administered two or more injections of the mRNA vaccines. HIV, Malaria, and Pertussis vaccines have also been reported to induce higher-than-normal IgG4 synthesis. 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****. 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.*

Repeated COVID-19 mRNA vaccination results in IgG4 class switching and decreased NK cell activation by S1-specific antibodies in older adults

https://immunityageing.biomedcentral.com/articles/10.1186/s12979-024-00466-9

Immune checkpoint inhibitors, often known as cancer immunotherapy agents, prevent checkpoint proteins from attaching with their associated polypeptides, allowing cytotoxic CD8+ T lymphocytes (CTLs) to attack cancer cells. Immune checkpoint-blocking (ICB) agents include anti-CTLA-4 (cytotoxic T-lymphocyte antigen 4) and anti-PD-1 (programmed cell death protein 1) monoclonal antibodies [87,88]. ICB has demonstrated therapeutic effectiveness in a wide range of cancer types, including advanced-stage cancer patients [89,90,91]. Regrettably, only 15–30% of cancer patients who have received treatment benefit from ICB's therapeutic efficacy [92]. Most crucially, new reports show that certain cancer patients receiving anti-PD-1 monoclonal antibody treatment have rapid disease progression (also known as hyper progressive disease (HPD) instead of cancer remission [93,94,95]. ***Notably, the PD-1 antibody belongs to the IgG4 family. Furthermore, cancers, such as malignant melanoma [48], extrahepatic cholangiocarcinoma [96], and pancreatic cancer [97], have been linked to plasma B-cell infiltrates that are IgG4-positive.*** *IgG4's contribution to cancer is poorly understood, but a groundbreaking study has added important new knowledge. Karagiannis et al. [48] studied malignant melanoma and found that IL-4 and IL-10 expression was elevated and that tumour-specific IgG4 was generated locally in the tumor tissues. It is common to think of IL-10 as an anti-inflammatory cytokine; however, this is only true in low quantities, as at larger concentrations, it shows pro-inflammatory effects [98,99,100].*

Karagiannis et al. [48] also found that, in contrast to cancer-specific IgG1, cancer-specific IgG4 failed to activate two immunological processes that employ antibodies to identify and destroy cancer cells. Moreover, the IgG1 antibody was able to suppress cancer progression in an in vivo model, while IgG4 failed to do so. IgG4 antibodies cannot directly attack tumour cells and can interfere with the process of tumour cell death mediated by IgG1 antibodies. The inhibition of IgG1 binding and activation by Fc RI is the mechanism behind this obstructing activity. Such findings point to a previously un-researched feature of tumour-induced immune escape: IgG4 synthesis induced by tumours limits effector immune cell activities against tumours [48]. Another work [101] came to the same conclusion; that is, the IgG4 antibody is important and necessary for cancer immune evasion. *In a cohort of individuals with esophageal cancer, B cells producing high IgG4 concentrations were markedly raised in malignant cells and also high in serum samples from patients.* ***More IgG4 seems to be linked to more aggressive cancer growth, and both were strongly associated with higher cancer malignancy and poor prognosis.*** *It was discovered that IgG4 can contend with IgG1 (as shown in Figure 3) in binding to Fc receptors present in some immune cells in vitro. This competition results in the inhibition of typical immune responses against cancer cells, such as cell and complement cytotoxicity and cell phagocytosis, which are mediated by IgG1 antibodies.*

Waning immunity and IgG4 responses following bivalent mRNA boosting

https://www.science.org/doi/10.1126/sciadv.adj9945

Studies have shown that COVID-19 mRNA vaccines and adenoviral-vectored vaccines induce preferentially IgG1 and IgG3, with limited IgG2 and IgG4 in both humans and nonhuman primates (20–22). ***However, recent longitudinal follow-up studies after a second or third monovalent mRNA vaccination showed evidence of some class switching toward IgG4 (23, 24). Further evolution of IgG subclasses after a fourth mRNA vaccination remains unknown.***

IgG subclass and functional responses following bivalent mRNA boosting

To explore in greater detail spike-specific antibody responses following bivalent mRNA boosting, we assessed IgG subclass responses (IgG1, IgG2, IgG3, and IgG4) against WA1/2020, BA.1, BA.2, BQ.1.1, and XBB.1.5 following bivalent mRNA boosting. Less than twofold increases in IgG1 responses were observed to WA1/2020, BA.1, BA.2, BQ.1.1, and XBB.1.5 at week 3 and returned to preboost levels by month 3 (Fig. 4AOpens in image viewer). A similar trend was observed with IgG3 responses. Slightly higher 4.9-, 2.7-, 1.9-, 1.7-, and 1.5-fold increases in IgG2 responses were seen to WA1/2020, BA.1, BA.2, BQ.1.1, and XBB.1.5 at week 3 (Fig. 4AOpens in image viewer). ***In contrast, markedly higher 11.2-, 11.0-, 9.1-, 8.5-, and 7.8-fold increases in IgG4 responses were observed to WA1/2020, BA.1, BA.2, BQ.1.1, and XBB.1.5 at week 3, and these responses were durable at month 3 (Fig. 4AOpens in image viewer). These results suggested that bivalent mRNA boosting did not substantially increase proinflammatory IgG1 and IgG3 responses but rather skewed responses primarily to isotype-switched IgG4 responses.***

A class switch toward IgG4 happens usually when an individual is frequently exposed to an antigen (19, 47), which was demonstrated in a study with beekeepers, where IgG1 antibodies specific to phospholipase A2, a bee venom antigen, class-switched to IgG4 after 6 months of continuous bee stings (48). Similarly, in the HIV vaccine trial RV144, where participants received canarypox vector–based HIV Env vaccines and purified HIV Env gp120 protein vaccines, elevated IgG1 and IgG3 antibodies correlated with enhanced effector functions, whereas in the clinical trial VAX003, where participants received seven doses of HIV Env gp120 protein vaccines, elevated IgG2 and IgG4 levels were observed with increasing boosts and correlated with inhibition of Fc effector functions (49–51). ***We speculate that a class switch from IgG1 to IgG4 might occur after multiple mRNA immunizations (23). This is also in line with an observation that class switch to IgG2 or IgG4 occurs more readily from IgG1 B cells (52), potentially to balance excessive inflammation, as IgG4 is known to have inhibitory effector functions***

Cytokine Storms and Anaphylaxis Following COVID-19 mRNA-LNP Vaccination: Mechanisms and Therapeutic Approaches

https://pmc.ncbi.nlm.nih.gov/articles/PMC11507195/

Recent reports have indicated that frequent mRNA vaccination may induce a gradual increase in TRAb levels and promote a class switch to IgG4, ***which could contribute to long-term immune responses and might be considered potential late-onset adverse reactions*** *[12,13]. Additionally, it has been suggested that* ***the use of 100% N1-methyl-pseudouridine (m1Ψ) in mRNA vaccines may pose a potential risk of promoting cancer development in the long term****, as m1Ψ has been associated with immune suppression and the facilitation of tumor growth and metastasis in certain models [14].*

mRNA vaccines against SARS-CoV-2 induce comparably low long-term IgG Fc galactosylation and sialylation levels but increasing long-term IgG4 responses compared to an adenovirus-based vaccine

https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2022.1020844/full

Instead, the mRNA, but not the adenovirus-based vaccines induced long-term IgG4 responses – the IgG subclass with inhibitory effector functions.

Nevertheless, all three vaccines seem to induce high protection from severe disease conditions in the next weeks after a second immunization (5, 18, 19), assuming a robust long-term systemic T and B cell response – also against non-RBD parts of the virus and virus escape variants (15). However, the influence of the different new vaccine formats with unclear co-stimulatory/"adjuvant" effects on the long-term B cell and Ab Fc response remains unknown.

IgG Fc-mediated effector functions are influenced by the induced IgG subclass and the IgG Fc N-glycosylation pattern. Human IgG1 and IgG3 subclasses have been described to convey the highest potential to activate immune cells via classical activating Fcγ receptors (FcγRs) and the classical complement pathway via C1q (20–24). These IgG subclasses can form hexamers, thereby facilitating the interaction with the six-arm C1q molecule (21, 25–29). IgG2 hardly interacts with classical FcyRs and C1q and its effector function-inducing capacity needs further investigation (20, 22, 23). In contrast, IgG4 shows higher affinity to the classical IgG inhibitory receptor FcyRIIB than to classical activating FcyRs (20, 22, 23). ***Furthermore, IgG4 cannot activate C1q but instead is able to disturb the hexamer formation of the C1q-activating IgG subclasses (21). Furthermore, IgG4 can generate Fab arm-exchange, meaning that heavy chains with different specificities can dimerize resulting in bispecific Abs, which reduces their ability to form immune-complexes*** *(30). Thus, IgG1 and IgG3 are the IgG subclasses with the highest potential to activate the immune system, whereas* ***IgG4 has less activating potential and can even inhibit the effector functions of IgG1 and IgG3.***

Exploring the possible link between the spike protein immunoglobulin G4 antibodies and cancer progression

https://www.explorationpub.com/Journals/ei/Article/1003140

However, after the second mRNA vaccine injection, an unexpected long-term side effect has been observed worldwide: a switch in the isotype of IgG antibodies took place. Before the emergence of these observations in the general mRNA vaccinated population, this phenomenon appeared to have been documented in single individuals and described as a rare vaccine side effect; either producing IgG4-related disease (RD) [9–13] or experiencing a relapse of IgG4-RD symptoms [14]. ***The phenomenon of rising IgG4 antibodies post mRNA vaccination has now been documented in studies involving human participants [8, 15–28] and at least one animal study [29]. It appears that the rate of increase of IgG4 antibodies can surpass all other IgG antibodies developed towards the spike protein, rising consistently from an average of 0.04% after the second immunization to 19.27% after the third one [8]****. This was echoed by another study, where the median level of IgG4 antibodies directed against the spike protein was 21.2% of all IgG antibodies [19]. In stark contrast, this phenomenon has not been reported in non-vaccinated individuals [16, 17, 23, 25, 27])*

Roles of immunoglobulin G4 (IgG4) antibodies in local immune escape. Under normal conditions, the IgG1 antibody recognizes the cancer-associated antigen. IgG1 then binds through the fragment crystallizable (Fc) to its receptor, located on the natural killer (NK) cells (shown) or macrophages

These are activated and NK cells release perforins and granzymes that destroy the cancer cell while macrophages phagocytose the cancer cell. ***However, when present, IgG4 could bind to the Fc region of the IgG1 antibody, thus inhibiting its union with its respective receptor located on the***

NK or macrophage cell. As a consequence, these effector cells are not activated and therefore cannot destroy the cancer cell.

Impairment of anti-tumour responses by immunoglobulin G4 (IgG4) antibodies engaging inhibitory FcγRIIB receptors. In normal circumstances, macrophages can recognize and eliminate cancer cells by phagocytosis. Tumours nevertheless continue to grow despite their presence. Some cancers have evolved immune evasion mechanisms, for example, by inducing over-expression of the fragment crystallizable gamma receptor IIb (FcγRIIB) receptor on macrophages. ***High levels of IgG4 could activate this inhibitory receptor (when the same cell is co-engaged with an activating FcγR receptor), inducing a state of anergy or even apoptosis of effector cells. It is hypothesized that IgG4 antibodies, by engaging FcγRIIB receptors located on macrophages can also impair anti-tumor responses, thus reducing their phagocytic functions.***

Class switch toward noninflammatory, spike-specific IgG4 antibodies after repeated SARS-CoV-2 mRNA vaccination

https://www.science.org/doi/10.1126/sciimmunol.ade2798

RNA vaccines are efficient preventive measures to combat the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic. High levels of neutralizing SARS-CoV-2 antibodies are an important component of vaccine-induced immunity. Shortly after the initial two mRNA vaccine doses, the immunoglobulin G (IgG) response mainly consists of the proinflammatory subclasses IgG1 and IgG3. **Here, we report that several months after the second vaccination, SARS-CoV-2–specific antibodies were increasingly composed of noninflammatory IgG4, which were further boosted by a third mRNA vaccination and/or SARS-CoV-2 variant breakthrough infections. IgG4 antibodies among all spike-specific IgG antibodies rose, on average, from 0.04% shortly after the second vaccination to 19.27% late after the third vaccination.** This induction of IgG4 antibodies was not observed after homologous or heterologous SARS-CoV-2 vaccination with adenoviral vectors. Single-cell sequencing and flow cytometry revealed substantial frequencies of IgG4-switched B cells within the spike-binding memory B cell population [median of 14.4%; interquartile range (IQR) of 6.7 to 18.1%] compared with the overall memory B cell repertoire (median of 1.3%; IQR of 0.9 to 2.2%) after three immunizations. This class switch was associated with a reduced capacity of the spike-specific antibodies to mediate antibody-dependent cellular phagocytosis and complement deposition. **Because Fc-mediated effector functions are critical for antiviral immunity, these findings may have consequences for the choice and timing of vaccination regimens using mRNA vaccines, including future booster immunizations against SARS-CoV-2.**

The appearance of anti-spike receptor binding domain immunoglobulin G4 responses after repetitive immunization with messenger RNA-based COVID-19 vaccines

https://pubmed.ncbi.nlm.nih.gov/38029832/

The seropositivity of anti-RBD IgG4 after the vaccination was 6.76% at 1 month after the second dose, gradually increased to 50.5% at 6 months after the second dose, and reached 97.2% at 1 month after the third dose. ***The seropositivity and titers of anti-RBD IgG1/IgG3 quickly reached the maximum at 1 month after the second dose and declined afterward.***

Repeated vaccinations induce delayed but drastic increases in anti-RBD IgG4 responses. *Further functional investigations are needed to reveal the magnitude of the high contribution of spike-specific IgG4 subclasses after repeated mRNA-based COVID-19 vaccinations.*

Conclusion

The majority of the journals which have covered this particular subject state that there is little research on the subject and more needs to be done especially in light of the amount of inoculations given worldwide from 2021. There has been a drastic increase in the people who have autoimmune conditions and cancer and while it would not be objective to associate these solemnly with the Covid-19 mRNA vaccine, the medical research is providing a strong link which warrants a much deeper investigation but only conducted free from conflict of interest and interlocks with the pharmaceutical industry.

I would like to see this issue raised in Parliament and something tangible be carried out rather than dismissed as controversial. It is the very least the public deserve to have a thorough investigation into the matter with transparency especially because these products still continue to be given to this day and are claimed to be completely safe.

Understandably this is a contentious issue but I believe that through reasonable debate and avenues for testing set up to find out who may have been harmed we can help restore the public's trust in the health services instead of the current situation which is spiralling ever more out of control as the days go by and the ubiquitous silence of the establishment continues.