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Review

Analysis of the capability of IgG antibodies and receptors with their relationships to food tolerance and autoimmune disorders

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Abstract

Recent research has shed light on a particular IgG mediated reaction that may serve as a natural defense mechanism against food-borne infections. The immune system has an unmistakable boundary when it comes to self-antigen intolerance. Tolerance establishment and maintenance to dietary antigens are critically impacted by IgG. Mutable auto immunological diseases are characterized by polyclonal antibodies and autoreactivity of B and T cells. Based on differences in the hinge area and the constant section of heavy chains, IgG subclasses are classified as IgG1, IgG2, IgG3, and IgG4. The ratio of IgG subclasses in serum is thought to be diagnostic of a particular autoimmune disease that causes autoantigens, according to various pieces of evidence. Through their regulation of interactions amongst Immunoglobulin Fc-gamma receptors, and complement, several studies have examined blood levels of IgG subclasses throughout the course of various illnesses, suggesting that they may play a pathogenic role. A high level of sub-neutralizing and cross-reactive non-neutralizing antibodies against viruses might accelerate the course of action of certain viral infections through a process known as antibody-dependent enhancement (ADE). The increased pathogenicity in ADE in vitro models has been linked to viral entry through the Fcγ receptor (FcγR) instead of the canonical viral receptor. Various viral diseases, including as dengue virus or SARS-CoV, are investigated in relation to FcγR engagement.

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Introduction: Adults with longer intervals between infections can be tested for lower levels of IgG class, whereas children with recurrent respiratory infections for 7 years can typically be identified with an IgG deficiency. During the pathogenesis generated by pregnancy hypertension, researchers have examined humoural immunity indicators, their interactions with inflammatory markers, renal functions, and angiogenic factors [1, 2]. In pregnancy-induced hypertension, which has been discovered to be self-regulating of many markers, the fluctuations in IgG levels and free light chains are evaluated. The free passage of IgG molecules between the placenta and the fetus, a decrease in their half-life due to recycling of lower systemic neonatal Fc receptors, and proteinuria are all associated with reduced IgG levels. On top of all that, pregnancy-related hypertension can also cause renal disorders and nephrotic syndromes. Hypogammaglobulinemia, caused by IgG leakage in urine during severe nephrotic syndromes, can occur because of the protein's large size [1].

Host, illness, and viral factors have shown that HIV-1 patients' IgG responses are regulated differentially, resulting in unique forms of neutralizer antibodies and non-neutralizer antibodies. Researchers found that anti-HIV-1 antibody responses were selectively antigen-driven and IgG subclass-dependent, and that all criteria strongly connected with amount of neutralization viral load and variety, ethnicity, and infection span predominated in these responses [3, 4].

Sub classes of IgG: IgG antibodies are the building blocks of the secondary immune response; they make up around seventy-five immunoglobulins in serum. There are four distinct subclasses of immunoglobulin G, with IgG1, IgG2, IgG3, and IgG4 accounting for66%,23%,7%, and 4% of the total IgG antigen the pool, respectively. Immunoglobulins of the IgG1-3 class can activate the complement system, whereas IgG4 does not. Similar to healthy individuals, patients with autoimmune diseases have been found to have different types of IgG subclass distribution in their serum [5, 6]. New evidence suggests that IgG antibodies may play a function in the immune system, which is an important finding. Results show an increase in IgG1 levels and decreases in IgG3 and IgG4 levels in patients with monoclonal gammopathies. On the flip side, IgG1 levels have been found to be significantly higher in multiple myeloma patients compared to IgG2, IgG3, and IgG4 levels [7, 8].

IgG1 is quite prevalent and has the ability to cross the placenta. The truth is that maternal serum levels are similar to neonatal ones, with the exception that levels decrease in the months following birth [9]. Decreased levels of the IgG1 subtype may explain hypogammaglobulinemia. illnesses of the respiratory tract are a common symptom of IgG insufficiency, and IgG1 deficient increases vulnerability to a number of illnesses. In a multivariate study, IgG1 did not seem be connected with hypertension caused by pregnancy [1]. With a serum level of 3 mg/mL in adults, the IgG2 subclass accounts for 20-30% of entire serum IgG. It seems that these antibodies work well against bacteria that have an outer membrane. When it comes to the humoral response to polysaccharide antigens, they are absolutely crucial. Multiple infections, including those caused by Bacteria pneumonia, Haemophilus influenza, and Neisseria meningitides, can affect people with IgG2 deficiency [10, 11]. One possible outcome of an inadequate blood IgG2 level following allogeneic hematopoietic stem cell transplant is late-onset pneumonia. Research has also shown that transplantation considerably lowers IgG and IgG2 levels when peri-transplant rituximab is administered. An increased risk of pneumonia was associated with lower IgG2/IgG ratios [12, 13]. A high IgG2 level in serum has been found to be linked with the course of many immune-mediated diseases. Immune system disorders, such as organ-specific. Because of the predominance of IgG2 distribution dependent on thyroid function, Hashimoto's thyroiditis and antithyroid peroxidase are serological hallmarks [14]. The serum IgG3 level reveals 4-8% of the total IgG class. Although these antibodies are powerful and proinflammatory, their short half-life restricts the extent to which they can cause inflammation. The typical progression of a viral infection is an increase in IgG3 levels, followed by an increase in IgG1 levels [15]. In patients with type III cryoprecipitates, it has been calculated that both IgG3 and IgG-RF are significant. Recent advances in our understanding of the immunological and evolutionary factors that contribute to mixed 7 cryoglobulinemia may be to blame. Consequently, a lower IgG3 level is associated with worse disease outcomes.

It appears that IgG3 at low temperatures can induce changed steric Ig, which in turn triggers cryoprecipitation in a reversible manner. It is likely that the main reason to trigger the long-term autoimmune Term immune process is the existence of IgG3 in HCV cryoprecipitates and antinuclear antibodies+ individuals [16]. In addition, it has been determined that IgG3 is likely associated with mixed cryoglobulinemia in HCV+ individuals' cryoprecipitates, indicating that the infection is occurring outside of the liver. Some have postulated that clonal selection may be related to CGs, in which case B cells are first stimulated to produce increased oligoclonal IgG3 clones with rheumatoid factor activity instead of IgG1 [17]. This theory of a harmful part of IgG3 within liver autoimmune illness is supported by the fact that Zhang et al. In primary biliary cirrhosis, found a substantially IgG3 levels are higher than in further autoimmune illnesses. [5]. With only 5% of the total IgG class present, IgG4 seems to be the least common of the IgG antibodies [18]. Since it lacks the ability to exert the aforementioned features of other subgroups of IgG, IgG4 is typically thought of as non-inflammatory and benign. The steric barrier of the Fc portion and the hinge region causes IgG4 to act in this way. Various investigations have shown that IgG4 connects with FcγR under certain conditions, despite its lack of immunological inertness. The Fc domain of IgG4 can attach to FcγRs, which can lead to negative consequences [19].

Chronic inflammatory demyelinating polyneuropathy, pemphigus, MG thrombotic thrombocytopenic purpura, and other autoimmune disorders are associated with IgG4, despite its apparent inertness. Various pathways are associated with IgG4 pathogenicity in this situation. To activate the complement cascade by an alternate channel,

such as the lectin pathway, experimental evaluations showed that IgG4 can impede enzymatic activity, such as protein-antigen interactions. It is worth noting that IgG4 consists of the Fc portion and the hinge region. Despite the great degree of commonality among IgG subclasses that a single amino acid variation can cause the complement system to no longer be able to activate immune systems [19, 20]. Chronic exposure to a non-infectious antigen can cause interleukins such as IL-13, IL-4, and IL-10 to generate IgG4 [21]. There was evidence that IgG4 demonstrated anti-inflammatory properties. Hence, it functions as a tolerance mechanism [22, 23]. Immunotherapy for allergies typically results in the dominant subclass IgG4 being elicited following prolonged exposure to stimuli in a non-infectious environment [24]. Immunotherapy symptom improvement seems to be associated with IgG4 expression [25]. Filariasis, in particular, stimulates the synthesis of IgG4, and greater quantities of circulatory IgG4 have been linked to asymptomatic helminth infections [25].

Positive correlation & disorders: A synergistic involvement of poly-specific IgG4 antibodies thru anti-filarial IgG4 in inhibiting disease progression in silent patients having microfilariasis has been suggested by the observation of a positive correlation among anti-filarial IgG4 with IgG4 against self-antigens [25]. Coincident with the identification of IgG4-RD, elevated levels of IgG4 were detected in the serum of individuals suffering from autoimmune pancreatitis associated extra-pancreatic lesions [26]. In their study, Kamisawa et al. [27–33] found that autoimmune pancreatitis patients had infiltrating IgG4-positive cells and suggested the term IgG4-RD for this entity. Specifically, type 2 autoimmune pancreatitis is known as idiopathic duct-centric pancreatitis while type 1 is called lymphoplasmacytic sclerosing pancreatitis. Elevated serum IgG4 levels identify type 1 autoimmune pancreatitis, which is a component of systemic IgG4-RD; type 2 autoimmune pancreatitis, on the other hand, is more commonly seen in younger individuals and lacks well-defined immune-mediated pathogenetic processes [34]. One possible diagnostic tool for IgG4-RD is the serum IgG4/IgG ratio [35]. The symptoms of IgG4-RD include mild to severe eosinophilia, storiform fibrosis in obliterative Phlebitis, high blood IgG4 concentrations, and pancreatic involvement, among many other possible organ effects [36, 37].

Higher level disorders: Higher stages of IgG4 may be connected with rheumatoid arthritis (RA) symptoms or treatment efficacy in RA patient role, according to certain research: This correlation may represent a distinct clinical phenotype defined by increased sickness activity, higher levels of autoantibodies, and worse therapeutic response, as demonstrated in an analysis of RA patients with elevated blood IgG4 levels by Chen et al. [36]. In addition, histological evidence of RA-typical synovitis was associated with an increase in synovial IgG4-positive cell populations, which in turn was associated with higher IgG4 [36]. In sum, additional research is required to elucidate the pathogenetic function of IgG4 in RA, and its function in the disease is still unclear. In MG, an autoimmune disease known as anti-acetylcholine channel (AChR) antibodies reduce the efficiency of neuromuscular transmission, which impacts the neuromuscular junction. A clinically established subtype of myasthenic glycosaminoglycan (MuSK-MG) is associated with anti-muscle specific protein tyrosine kinase (MuSK) antibodies, which are present in a large proportion of myasthenic people who do not have anti-AChR antibodies. Disease severity and responsiveness to treatment are also correlated with MuSK antibodies [38]. According to research by Niks et al. [39], which looked at the relationship between illness severity and antiMuSK specific IgG subclasses, the only subclass connected to disease severity was IgG4. Notably, in vitro with refined IgG4 and in laboratory animals via indirect transfer of refined IgG4 indicated that the deleterious effect of MuSK antigens was nearly exclusively mediated by the IgG4 subclass [40-43]. The sole case of MuSK-MG with lymphadenopathy and IgG4-RD histopathology that we are aware of so far is a patient who responded very well to B cell reduction but whose blood IgG4 levels remained high. According to recent findings, which show that anti-CD20 depleting therapy selectively targets specific MuSK IgG4 while having no effect on total IgG4, it is likely a particular anti-MuSK antibodies only make up a small percentage of total IgG4 [44]. The connection between MuSK-MG to IgG4-RD needs to be further investigated. There is new evidence linking celiac disease to a specific increase in serum IgG4. While definitive evidence of this has not yet been found, there is some evidence that IgG4 is involved in the immune system's response to various protein antigens found in food (e.g., [14, 29]) and that the intestinal Peyer's patches contain a disproportionately high concentration of IgG4-producing cells (e.g., [45]). Rare studies on IgG subclasses in liver transplant recipients have shown promising results: pancreatic-cholangiopathy response to corticosteroids is associated with elevated serum IgG4 levels post-transplant. There seems to be an association between rejection and liver transplant loss and the presence or expansion of donorspecific IgG3 ahead of to or after transplantation. Although it is unclear whether conventional immunosuppressive regimens alter the humoral response, The study reveals a notable reduction in the production of all IgG subclasses post-transplantation, especially in conjunction with tacrolimus and sirolimus. Future investigations into the implications of IgG subclass responses in liver disorders and transplant scenarios hold significant promise and lead to the discovery of new personalized therapeutic mechanisms [46].

Disorders: On the flip side, elevated IgG1 levels are common in thyroid disorders [47]. During the initial phase of Hashimoto's thyroiditis, referred to as the euthyroid stage, immune dysfunction initiates without evident symptoms. The condition is categorized by persistent follicular destruction, and inflammation, requiring around 90% involvement of thyroid gland to trigger hypothyroidism. In sera of patients with Hashimoto's thyroiditis, the most common subclasses of TPOAb were IgG1 and IgG4. Hypothyroidism, in its most severe form, may be more likely to occur in patients with elevated quantities of TPOAb IgG2 is and IgG4 subtypes [14]. There has been a recent description of a strong correlation between IBS (irritable bowel syndrome and isolated

increased blood IgG2 levels, which supports the idea that patients with isolation IgG subclass increases should be further investigated for illness correlations [45]. Patients with irritable bowel syndrome (IBS) who also had a Blastocystis hominis infection had higher serum IgG2 concentrations, which may indicate that the parasite's carbohydrate antigens play role in development of disease [48].

Ratios of IgG subclasses: Patients with chronic lung disease that is obstructive are at increased risk for exacerbations and/or admissions if their levels of certain IgG subclasses, for example IgG2 and IgG1 are low, according to a new paper from the Canadian Respir Research Network [49]. Chapter 6, Napodano et al. [20]. Yamazaki et al. assessed serum total IgG levels as a marker in allogeneic hematopoietic stem cell transplantation recipients, specifically focusing on the heightened susceptibility to infectious complications during the early post-transplant period, pre-neutrophil incorporation, and up to two years' post-transplantation [12, 13]. Recent studies have shown that patients with chronicle lymphocytic leukemia who do not produce enough IgG1 (and IgG3) have a lower chance of surviving the disease and surviving treatment-free. Immune dysfunction in CLL is not constant, and Ig levels are correlated with the length and stage of the disease [50]. A greater prevalence of each solitary and repeated Ig and IgG subgroup deficiencies may be observed in patients with advanced illness stages at the stage of Ig testing, according to these observations. Impairment of the immune system is associated with more severe disease and may serve as an indicator of the need for therapy. In these patients, tracking Ig levels can be useful since they show how the disease is progressing [51]. Pregnant women who have hypertension (pre-eclampsia) also have significantly lower blood IgG1 (and IgG3) levels [1]. A recursive based on proteins falciparum vaccine (RTS, S/AS01B) was found to protect newborns and young children against the disease, according to recent reports [52]. This protection was mediated by particular IgG subclass responses, primarily IgG1 and IgG3. Malaria vaccine efficacy remains below the 75% target set by the Global Health Organization, which is an interesting fact [53]. Recently, Kurtovic et al. showed that antibodies against Plasmodium falciparum sporozoites can be produced through testing inoculation with sporozoites or antibodies that humans naturally acquire [54, 55]. These antibodies can activate the conventional complement pathway and promote obsessive of the complement factor C1q.

Human immunodeficiency (HIV) infections often include the IgG1 subclass of antibodies, albeit this might vary with HIV antigen type, illness stage, and vaccination schedule [56]. IMMUNOLOGICAL INVESTIGATIONS 5 Among all antigens, IgG1 responses are the most reactive, followed by IgG3 and IgG2. Conditions fostering a shift to IgG1 subclass, increased rate of recurrence of IgG1-specific cells, or heightened IgG1 production collectively contribute to elevated IgG1 levels. The serum IgG1 (IgG1/IgG) or IgG3 (IgG3/IgG) levels were found to be significantly higher in patients with primary biliary cholangitis (PBC), systemic sclerosis (SSc), primary lupus erythematosus (pSS), and primary biliary the condition (pSS) compared to healthy individuals. The authors of the study also identified unique features of each immune-mediated illness group [5].

Of the 28 patients diagnosed with autoimmune loss of sensorineural hearing, 46.4% had a subnormal pattern of IgG1 or IgG3 subclasses, which is defined as an amount below the relevant lower reference range [57]. In a recent study by Basile et al., the investigation focused on contrasting IgG subclass level among individuals having myasthenia gravis (MG), healthy blood donors and additional autoimmune diseases. The findings revealed a noteworthy elevation in mean serum IgG1 levels exclusively in individuals with systemic autoimmune diseases, distinguishing them from both the MG and healthy groups [58]. These findings provide more evidence that the distribution of serum IgG subclasses may exhibit unique features in certain autoimmune disorders. Although interferon gamma, or a key th1 cytokine, can trigger IgG2 synthesis and source an increase in serum IgG2, it has been demonstrated that in Hashimoto's thyroiditis, the majority of T helper (Th) cells entering the gland that houses the thyroid are Th1 cells. There may be an increased risk of developing frank hypothyroidism when IgG2 levels are high [59].

Food Allergy: An aberrant and immunologically conditioned sensitivity to certain foods is known as food allergy. Although the first requirement of food allergy is satisfied by immune reactions through specific IgG antibodies produced towards food antigens, the second requirement is not satisfied because the reactions are still considered normal reactions linked with exposure to food antigens. According to what is known currently, the immune system views foods that trigger IgG-mediated responses to dietary antigens as potential infections. Instead of talking about sIgG antibodies as a cause of hypersensitivity, we should talk about them as a sign of immunological tolerance linked to regulatory T cell activation. Laboratory tests that rely on sIgG titrations against foods are not useful for diagnosing food allergies or intolerances, and they should not be conducted when symptoms related to food are present [60]. Twelve healthy adults participated in a study that tested their sIgG4 levels in response to nine typical foods: pork, eggs, nuts, grain flour, banana cultivation, orange, rice, and potato. It appears that these antibodies are created as a natural aspect of exposure to food, since none of the participants reported any symptoms after consuming the examined goods, even though all of them had sIgG4 against the foods that were studied [60].

Defence mechanism to food allergens: Under normal circumstances, antigens cannot penetrate the intestinal tract epithelium. However, when this barrier is broken due to inflammation, antigens are able to come into touch with immune system cells. This interaction triggers immunization and the manufacture of specialized defense IgG antibodies. Defense reactions are triggered when these antibodies come into touch with the antigen. This involves the formation of immunological complexes between the antigen and the antibodies, the activation of the complement protein cascade, and effector cells such

neutrophils, lymphocytes, macrophages, eosinophils, and platelets. Consequently, the reticuloendothelial system phagocytoses and subsequently destroys the immune complexes. In addition, the inflammatory response that occurs as a result of the immunological connection between sIgG and meal antigens may make the gastrointestinal mucosa even more vulnerable to further injury and increased permeability. Consequently, the existence of particular IgG antibodies that target food allergens is a reflection of the body's natural defense mechanisms in response to allergens that penetrate the epithelial barrier. As a part of its particular humoral response to infections, the immune system primarily relies on IgG antibodies as its first line of acquired defense [61]. The findings of a study by Zuo et al. [62] that compared the levels of sIgG against fourteen food allergens in a group of healthy individuals with those in a group of patients with a condition known as and functional dyspepsia lend credence to this idea. The existence of specific immunoglobulin G (sIgG) antibodies against dietary antigens was established in all patients of both research groups and controls.

Intolerance to food antigens:

Treg Cells: These cells are dendritic cells in particular. iTreg cells migrate to the lamina propria of the intestinal epithelium, CD103+ cells go to lymph nodes and induce T cell development into iTreg cells, while CX3CR1+ cells are non-migratory and subepithelial [63-66]. In this context, they interact with CX3CR1+, leading to the expansion of antigen-specific iTregs. It leads to a dampening of allergic reactions, which include dampening of Th1 and Th2 balance, IL10 release, suppression of IgE and effector cells (including basophils, eosinophils, and mastocytes), and induction both IgA and IgG4 [63].

Skin Allergy by food: Some 73 patients who reported skin problems and linked them to food consumption were studied by Antico et al. Rash, skin irritation, and redness were the symptoms that were described.

SlgG & slgE: We tested every patient against food and inhalation allergies by skin tests, measured their sIgE and sIgG levels, and then had them participate in open oral incitement challenges with foods that tested positive for sIgG. If they passed, they then participated in a double-blind placebo-controlled food testing (DBPCFC) with the same foods. Only 38 individuals had sIgG4 antibodies to foods, while 7 had both sIgG4 and sIgE. No evidence of food-specific IgG was found in the other 28 individuals. No one in the 45 patients tested for sIgG4 in the DBPCFC experiment developed an aversion to the foods that tested positive. Conclusion: titrating sIgG4 in adults does not help with clinical an allergy to food or intolerance diagnosis, according to the scientists. When diagnosing and treating adult patients with skin problems associated to allergies, the titration levels sIgG4 shouldn't have to be included [67]. High sIgG4 values are linked to asymptomatic sensitization and successful immunotherapy, suggesting that these antibodies may play a protective or blocking role, to summarize the associations between the sIgG with sIgE antibody [68]. Sensitizing foods are better tolerated by children whose sIgG4 for sIgE ratio is high [69]. One indicator of eventual tolerance in infants with IgE-mediated allergies is a high sIgG level [70].

Ratio of IgE & IgG subclasses in food allergy: The secretion of allergen-specific antibody types IgE is elevated in patients with Igg-mediated food allergies, but the generation of allergen-specific IgG1 or IgG4 antibody responses is minimal or nonexistent [71, 72]. Reductions in sIgE and increases in sIgG4 are common side effects of oral immunotherapy, according to studies. One mechanism by which immunotherapy causes an upregulation of allergen-specific IgG4 is by reducing basophil activation and blocking the binding of particular IgE to their receptors [63]. Patients with an IgG-mediated allergy showed far higher levels of IgG than those with an IgE-mediated allergy, but those in the healthy group who were tolerant to milk did not vary [73]. It is emphasized in the Worldwide Consensus ON (ICON) record on food allergies, which was prepared by the World Allergy Organizing (WAO), the American Board of Allergy, Asthma and Immunology (AAAAI), and the European Association for Allergy and Asthma (EAACI) [74], that specific IgG titration against food items is not a suggested test for food allergy diagnosis.

Hybrid IG4: The whole antibody can bind to particular allergens or germs since lighter chains have variable sequences. Human IgG4 proteins are quite malleable; they can undergo half-molecule exchanges in vitro to transform from monovalent antibodies that bind to a single antigen and into bi-specific antibodies that bind to two distinct fragments [75, 76]. Heavy chains connected weakly by noncovalent interactions make up around half of the molecules of IgG4. New disulfide bonds are formed at the hinge region as a result of this process, but the heavy-light chain disulfide connection is not disrupted [77]. When the heavy chains of an IgG4 molecule do not form disulfide bonds, the noncovalent bonds can dissociate, allowing the chains to randomly separate and rejoin (Fab-arm exchange) [78] [79]. Therefore, it is possible for an IgG4 molecule to have both κ and λ chains, creating an asymmetrical or "hybrid" Ig with two distinct antigen-binding domains (Figure 2). According to experimental evidence, this molecule may have a physiological function, as hybrid IgG4 κ/λ constitutes a significant fraction of IgG4 in regular human serum. Unlike naturally occurring four-molecule hybrids, synthetic compounds lack the ability to cross-link antigens or trigger lymphoid-responses, therefore dampening inflammatory response [77]. An Ig strong chain (α, δ, γ, ε, or μ in human) linked to one type of the light chain (λ or κ) is what makes up the typical antibody, which is made by single developed plasma cell. The antibody class is determined by the kind of heavy chain; antibodies can be either IgA, IgD, IgE, IgG, or IgM. There are two parts to every heavy chain: the constant and variable regions. In addition, there is always one type of illumination chains, λ or κ, present in each antibody in animals [9, 80]. Each antibody also contains two identical light chains.

Fcγ receptor: The FcγR family members stimulate the effector cells to react that are crucial for the host's defense against infection, whereas the Fab component of an IgG antibody binds with viral targets and can impede the virus's

entry, fusion, or maturation, thus neutralizing the virus. Dissimilarities in the major amino acid sequence among IgG subclasses (IgG1-IgG4 in humans) and the structure and substance of the Ff-associated glycan complex dictate the binding specificity and affinity of its Fc domain for various FcγRs [81-86]. The diversification of Fc domains is driven by these two factors, and the end result is IgG Fc domains that can engage and activate multiple species of the FcγR group that are expressed by functional leukocytes [68].

Fc effector: The effector functions mediated by FcγR are varied and intricate. Nevertheless, progress in Fc domain engineering either the likelihood of animal strains that mimic the distinct characteristics of human FcγR physiology138, and the presence of pathogenic Fc receptors have resulted in the protection of FcRs through humoral and innate immunity. The rapid elimination of infected cells and opsonized virions with phagocytic and cytotoxic systems, as well as the induction of responses from the adaptive immune system through modifying of dendritic cell function67, are outcomes of diverse protective activities linked to activated FcγRs, which have antibodies that combat viruses and downstream signaling. The antiviral activity of IgG antibodies is mainly due to their ability to activate specific FcγR pathways on certain immune cell populations, which are crucial for mediating Fc effector functions, according to a lot of research from genetic association studies and in vivo experimental systems [87-96]. It has been found that blocking Fc-FcγR interactions greatly reduces the antiviral protection that even the strongest neutralizing mAbs can provide in vivo. On the other hand, mAbs that don't work well in in vitro tests can still offer strong protection against viruses in vivo, indicating that the antiviral protection that these mAbs provide relies on activating FcγR participation [87-94, 96]. Despite being over 90% identical in their constant regions, the four subclasses of IgG can differ greatly in their effector roles and antigen affinity. As a result, IgG subdivisions differ in their ability to trigger inflammatory response due to their differential interactions with complement as well as FcγR [97]. Important amino acid residues that mark the empathy of region known as Fc for FcγRs and for complementing component have been identified in research that try to improve the effector actions of healing antibodies [98]. There is a newfound fascination with IgG subclasses due to the enhanced function of FcγR in the result of inflammatory immune system outcomes. An individual's vulnerability to illnesses that are infectious, response towards antibody-based treatments, and autoimmune human diseases can be influenced by mutations in the FCGR gene, which can impact how it works through IgG subclasses and, ultimately, the deposition of immune complexes [99]. It has been shown in multiple studies that antigen characteristics may control and direct the synthesis of each IgG subtype [5, 98]. Because different isotypes of IgG have distinct biological and functional characteristics, the distribution of subclasses may control the course of autoimmune and immune-mediated illnesses [100].

Conclusion: This review aims to provide illustrations of IgG distribution in case of various immunological illnesses, with a focus on disease causation. Everything said so far points to the fact that the ratio of antibodies found in various organs has nothing to do with the concentration of IgG subclasses in serum. European Association of Allergology and Clinical Microbiology shown that IgG4 titration is not a reliable method for determining if a person has a food allergy. It has been discovered that levels of IgG subclasses can be used as a predictor to evaluate the maturation of complicated B cell immune responses. Therefore, in this age of precision medicine, this evaluation can serve as a standardized instrument for "immunological fingerprinting" in the administration of patients' customized medications and the early detection of disease. On top of that, it's useful for disease prognosis. The molecular and cellular processes that govern the IgG profile may be pivotal in the development of immunogens and therapies that improve immunity and lessen the impact of autoimmune responses. At this time, there is no universally accepted method for determining IgG subclass quantities. As a result, it's not easy to compare data from different tests due to variations in calibration and different reference intervals. Due to their unique immunological properties, IgG subclasses have shown promise as a marker to regulate the complex development of the B cell the immune system's response. So, in this age of precision medicine, evaluating IgG subclasses is a promising tool that might usher in a new era of patient-specific medication treatment: which can contribute to concept of an illness-related "immunological fingerprint" that might prove invaluable in early disease detection and prognosis. The creation of anti-SARS-CoV-2 mAbs could be guided by previous work on Fc-engineered mAbs, which could activate certain FcγR pathways on different types of leukocytes selectively, leading to better therapeutic efficacy.

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