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Commentary

Academic dissertations and scientific accountability: A critical appraisal of *Durable Immunity Against SARS-CoV-2 Omicron: Booster Vaccination and Hybrid Immune Responses*

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Abstract

This editorial critically examines the ethical considerations and methodological approaches presented in the dissertation *Durable Immunity Against SARS-CoV-2 Omicron: Booster Vaccination and Hybrid Immune Responses*, defended by Milja Belik in 2026 in Turku, Finland. Biomedical research should be guided by scientific integrity rather than by transient political influences. Given the profound impact of biomedical research on public health policy, clinical practice, and scholarly communication, adherence to rigorous methodological standards and critical scientific evaluation is essential. Furthermore, the uncritical acceptance of politically influenced claims may have broader implications, as such material may contribute to the training of artificial intelligence systems that could subsequently influence medical education and scientific discourse. Several aspects of the dissertation that warrant critical examination are identified. Among the principal concerns are the conclusion that hybrid immunity provides greater protection than naturally acquired post-infection immunity and the recommendation for repeated booster vaccinations. The potential induction of tolerogenic IgG-class antibody responses following multiple immunizations is not considered. The difference in immune response after lipid nanoparticle (LNP)-based immunization and after natural SARS-CoV-2 infection, noting that LNPs lack the cellular receptor specificity that characterizes viral infection, is essential. Likewise, the conclusion that repeated immunizations do not result in T-cell exhaustion is insufficiently demonstrated. The study design, highlighting the limited sample size and the six-month follow-up period after repeated immunization of healthcare workers (HCWs) to prove that T-cell exhaustion does not occur, is an important methodological limitation. The description of participation as voluntary was misleading. Overall, several methodological assumptions and interpretations require more comprehensive justification.

Introduction

Doctoral dissertations in medicine represent original scientific contributions and may influence future research, public health policy, and medical education. Consequently, they should remain open to rigorous scientific scrutiny and critical evaluation. The purpose of scientific discourse is not only to disseminate new knowledge but also to examine the validity of cotemporally scientific methods, the unbiassed interpretation of findings, and the strength of the conclusions drawn from the available evidence.

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In December 2025, concerns regarding the scientific methodology and interpretation of the doctoral dissertation *COVID-19 Vaccine Effectiveness in Finland During the Pandemic: Register-Based Cohort Analyses*, defended by Eero Poukka at the University of Helsinki, were submitted to the Dean of the Faculty of Medicine, the Chancellor of the University of Helsinki, and the official opponent. The Chancellor concluded that the concerns did not warrant further investigation. Nevertheless, the questions raised regarding the interpretation of vaccine effectiveness remain, in the opinion of the present author, matters of legitimate scientific debate. Using the official sites and peer-reviewed publications it was found that the "effectiveness" of the COVID-19 vaccines in children cannot be proven [1].

The present editorial addresses the academic dissertation "Durable Immunity Against SARS-CoV-2 Omicron: Booster Vaccination and Hybrid Immune Response" (available from: UTUPub [2].

This dissertation is based on three separate publications, each of them co-authored by 19-25 Finnish biologists and medical doctors.

The objective of this editorial is not to review the extensive literature concerning COVID-19 vaccination. Comprehensive reviews of this subject have already been published. Rather, the aim is to critically evaluate the scientific methodology, interpretation of the results, and conclusions presented in this specific doctoral dissertation. Because doctoral dissertations may subsequently influence scientific literature, public health policy, educational material, and artificial intelligence systems trained on published scientific sources, critical evaluation of their scientific rigor remains an important component of academic discourse.

The organization of this editorial follows the structure of the dissertation to facilitate direct comparison between the original text and the present critique. References to the relevant pages of the dissertation are provided throughout.

Conceptual considerations regarding hybrid immunity

One of the principal questions addressed by the dissertation concerns the concept of hybrid immunity. The dissertation concludes that hybrid immunity provides durable protection against SARS-CoV-2 infection. However, the rationale for considering hybrid immunity superior to naturally acquired post-infection immunity is not demonstrated.

Natural infection induces immune responses against multiple viral antigens, including the Spike, nucleocapsid, membrane, and envelope proteins, thereby generating a broader repertoire of humoral and cellular immune responses than vaccination directed exclusively against the Spike protein. Natural infection produces immune response towards a much broader antigenic stimuli, not only to the Spike protein but to nucleocapsid, membrane and envelop proteins of the alleged virus thus creating a broader repertoire of immunoglobulins and T- reactive lymphocytes [3]. The potential implications of these immunological differences for the durability and breadth of protective immunity warrant reassessment of COVID-19 vaccine benefit.

Similarly, the term *durable immunity* is used throughout the dissertation without a precise definition of the duration or immunological criteria by which durability is evaluated. The rationale for repeated booster immunization following recovery from natural infection is also not critically examined. These conceptual issues are central to the interpretation of the dissertation's conclusions and therefore merit more comprehensive discussion.

According to Section 2.4.3 of the dissertation (p. 32), "Hybrid immunity refers to the immunity acquired after SARS-CoV-2 infection that occurs after one or more doses of COVID-19 vaccines, also known as a breakthrough infection, or vice versa". In other words, hybrid immunity is defined as immunity acquired through a combination of SARS-CoV-2 infection and one or more doses of a COVID-19 vaccine, irrespective of the sequence of these events. This definition raises several questions. First, the frequency and clinical significance of breakthrough infections in the vaccinated cohort are not discussed in relation to comparable data from unvaccinated individuals. Second, the immunological rationale for vaccination following recovery from natural infection is presented without critical consideration of the available evidence supporting this approach.

The discussion in the dissertation lacks critical assessment of the appropriateness of vaccination during a period of widespread transmission of an infectious agent. The possibility that vaccination during an ongoing epidemic may contribute to a selection pressure, triggering the evolution of potentially more virulent viral strains or the variants with increased fitness, e.g. increased transmissibility was not addressed.

Immunological pathways of mRNA vaccination are different from natural infection

A central premise of the dissertation is that vaccination elicits immune mechanisms that closely resemble those induced by natural SARS-CoV-2 infection. This assumption forms the basis for several of the dissertation's subsequent interpretations. However, the biological equivalence of these two processes is not justified.

The dissertation states (p. 12) "COVID-19 vaccines are designed to elicit humoral and cell-mediated immune responses by presenting the SARS-CoV-2 spike protein antigen, thereby mimicking natural infection without causing disease. . . .". While both vaccination and natural infection may induce adaptive immune responses directed against the spike protein, important biological differences exist between these two modes of antigen exposure.

The intramuscular introduction of lipid nanoparticles (LNP)-formulated modified mRNA is not similar to natural infection, as it neither occurs via mucosal entry nor follows the same receptor-mediated cellular targeting pathways. In other words, the potential for non-specific cellular uptake drastically distinguishes it from the natural infection.

In natural infection, the virus enters permissive cells through receptor-mediated mechanisms (PRRs, pattern recognition receptors) involving host cell recognition pathways. By contrast, modified RNA in vaccines is delivered as cargo by LNP vehicles. These synthetic lipid structures lack specificity for naturally occurring cellular receptors (PAMPs, pathogen-associated molecular patterns). Instead, LNPs due to their lipid composition can fuse with cell membranes of any cell, allowing mRNA entry into a wide range of cell types. This process lacks cellular specificity characteristic for natural viral infection.

Consequently, the cellular distribution, kinetics of antigen expression, and immunological context of antigen presentation may differ substantially between natural infection and mRNA vaccination.

The dissertation does not discuss the implications of the broad tissue distribution reported for LNPs following intramuscular administration. If multiple cell types express spike protein after mRNA uptake, all these cells may, in principle, become targets of cytotoxic $CD8^+$ T-cell

responses following presentation of spike-derived peptides through major histocompatibility complex class I pathways. The potential consequences of this mechanism for tissue-specific inflammatory reactions are not considered in the dissertation.

Furthermore, the possibility that modified mRNA may produce spike protein for uncontrollable periods following vaccination is not discussed. The duration, tissue distribution, and quantity and quality in terms of folding/misfolding of spike protein expression remain important biological variables when evaluating immunogenicity and safety. Their potential influence on immune responses deserves more comprehensive discussion than is provided in the dissertation.

The common knowledge is that modified mRNA incorporates pseudouridine to enhance translational efficiency and reduce innate immune sensing. Whether these molecular modifications influence antigen processing and presentation in ways that differ from natural infection remains unclear. These mechanistic considerations are relevant when assessing the extent to which mRNA vaccination can be regarded as immunologically non-equivalent to natural infection.

Repeated vaccination and cumulative antigenic stimulation

The dissertation concludes that repeated booster vaccination contributes to durable immunity and enhanced immune protection.

Breakthrough infections are acknowledged throughout the dissertation. Nevertheless, the immunological implications of repeated sequential exposure to spike protein through vaccination followed by infection, or *vice versa*, are emphasized as an acceptable public health practice. The cumulative antigenic burden associated with multiple immunizations combined with subsequent infections is not discussed, despite its potential relevance to overstimulation of immune system with consequent sequalae of inflammatory and hyperimmune or autoimmune reactions.

Antigen presentation and the role of cytotoxic T cells

Taking this into account, one could hypothesize that multiple cell lineages may take up mRNA and thus convert into a factory production of toxic non-self-spike protein therefore becoming targets for the attack by circulating cytotoxic $CD8^+$T-cells. Whether or not spike-derived peptides manufactured from mRNA delivery is processed and presented via MHC class I pathways, like the presentation during the natural infection, is a question given the substantial differences in the entry mechanisms and the amount of the antigenic load. Also, because of the possibility of the frameshift in the spike protein translation (due to the methylated uridine in the modified RNA) the presentation of the peptides [4] may be compromised, therefore, not completely resembling the natural antigen presentation.

If a broad range of cell types were to express spike protein, these cells could, in principle, become targets for cytotoxic $CD8^+$T-cell responses. In such a scenario, various tissues including endothelial cells and myocytes are affected. This is not merely a theoretical concern but has been documented in multiple clinical publications describing postvaccine myocarditis and intravascular clotting.

In the literature, the potential cumulative antigenic burden associated with repeated exposures to the spike protein, whether through multiple vaccinations accompanied with breakthrough infections may cause overwhelmed hyperimmune reactions. The concept referred in the literature to as “spike protein-related toxicity, or spikopathy” [5], the possibility of inflammatory reactions associated with cumulative and prolonged production of non-self, toxic Spike protein in very high quantities and the basic principles of toxicology were not addressed. This discussion would have strengthened the scientific balance of the dissertation.

Tolerogenic IgG4

Immunoglobulin class switching from IgG1 towards tolerogenic IgG4 following repeated mRNA vaccination [6] which can occur already after the second immunization dose was not discussed. Because IgG subclasses differ in their biological properties, including complement activation and F_c receptor interactions, their potential relevance to vaccine-induced immunity warrants caution. Also, as is well known, IgG4-class antibodies may be monovalent (although possessing neutralizing activities) in comparison to the divalent IgG1 antibodies.

Study design to test cell mediated immunity in Health Care Workers

The dissertation provides limited clarity in its description of study participants. The research appears to rely on blood samples collected multiple times (up to 13 venipunctures, Fig 5, p. 36) from healthcare workers (HCW). It was stated that HCW voluntarily participated in the study. It reads (p. 35) “written informed consent was obtained before collection of the first study sample”. However, it is not clear whether HCWs participated voluntarily for multiple venipunctures depicted in Fig 5. Importantly, it has not been mentioned that HCW were mandated to get vaccinated. To facilitate this illegal intervention, paragraph 48a was added to the Law of Communicable Diseases (in Finland) and later removed under the pressure of the public. Therefore, it is incorrect to claim “voluntarily” in the context of HCWs.

From Fig. 11 (page 53) we can see that the observation period was at its best only 6 months after the 4th vaccination. Why did the dramatic drop in the number of observations at the 6-month time point occur being only n=5-6? Of note, 37 out of 111 participants (33%) with severe or moderate immune disorders were excluded from receiving the 4^{th} dose.

No demonstration of the lack of T- cell exhaustion

In the conclusion Section (p.79) of the dissertation the claims that multiple vaccinations and breakthrough infections will cause robust T-cell responses without cell exhaustion was not proven. It reads ”Two vaccine doses already provide strong T-cell immunity. T-cell responses are not exhausted by repeated vaccinations, but they do not necessarily expand the antibody response further. Therefore, booster vaccines should be updated to match circulating variants to reduce the impact of multiple SARS-CoV-2 infections”.

The observation period of 3 months only seems to be too shot to claim the lack of T-cell-exhaustion. Moreover, the absence of the T-cell exhaustion was not documented by stimulation with irrelevant antigens, e.g. derived from influenza, parainfluenza viruses or adenovirus. Therefore, the containment of robust protection against other respiratory viruses was not demonstrated.

To conclude, the reviewed dissertation seems to lack objective approach and was done on a demand to justify the policy of mandating and coercing HCW many of whom received injuries and some were badly disabled. We do need a real scientific debate in Finland concerning the level academic dissertations that seems to be tailored to support political decisions.

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