Reply to “Innate immune suppression by SARS-CoV-2 mRNA vaccinations: The role of G-quadruplexes, exosomes, and MicroRNAs”: Important concerns on the validity of this article.

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Dear Editor,

You recently published in “Food and Chemical Toxicology” an article from Seneff et al. entitled “Innate immune suppression by SARS-CoV-2 mRNA vaccinations: The role of G-quadruplexes, exosomes, and MicroRNAs” [1]. We show in this Letter that this article contains several fallacious scientific assumptions leading to misunderstandings and thus invalidating the conclusions drawn by the authors. We suggest that the article be retracted since a careful analysis of the provided bibliography indicates profound misinterpretations of topics and conclusions about the negative impact that vaccination against SARS-CoV-2 could have on immunity.

In the abstract, the authors claim that they will provide "evidence that vaccination induces a profound impairment in Type I interferon (IFN) signaling, which has various adverse consequences to human health". This statement relies on an unpublished preprint available on MedRxiv since August 2021, thus not yet peer-reviewed.[2] Data show a differential gene expression profile in peripheral dendritic cells based on vaccinal status, but do not support the authors’ claim that there is Type I IFN suppression due to the vaccine. Reliable research shows this is simply the reaction expected from a vaccine: a high immune response without a systemic and uncontrolled inflammation.[3 4 5] Furthermore, arguing that SARS-CoV-2 vaccination would result in loss of the Type I IFN immune response (and therefore leading to a higher infectious risk or lack of cancer surveillance) contradicts other published data on the immune response.[6] At the opposite, a transient increase of Type I IFN could explain some immune side effects caused by vaccination.[7 8] To date only a set of SARS-COV-2 viral proteins have been shown to antagonize Type I IFN response, not the vaccine.[9 10 11]

Furthermore, the authors used more than 200 references, including misunderstandings of other authors’ conclusions. To illustrate our point, in Table 1, we detail a non-exhaustive list of such misunderstandings of the literature. The authors rely on hypothetical physiological disturbances induced by vaccination. For example, they suggest a possible increased risk of various cancers which has never been published so far, whereas for patients with cancer, vaccination is still highly recommended [1213]. No causal relationship can be established between the described biological mechanisms and the alleged effects of mRNA vaccines in this article. The misuse and the erroneous interpretations which can result from the VAERS (Vaccine Adverse Events Database) database has been extensively described.[14 15 16] Besides, the analysis proposed by the authors only takes into account the relative values of the occurrences of several adverse events

for SARS-COV-2 or non- SARS-COV-2 vaccines without taking into account either the number of injections for each vaccine or the differences in pharmacovigilance. Thus, no conclusion can be drawn from this analysis. To date no published analysis of the data from the VAERS database supports the hypothesis of a significant increased mortality secondary to vaccination [17], confirming that anti-SARS-CoV-2 vaccination has a very favorable risk-benefit ratio and saved and will save lives.[18 19]

The review of important paragraphs has highlighted major shortcomings and blatant approximations in the usage of the literature which, in fact, goes against all the assumptions made in the manuscript. The entirety of the scientific and medical community is concerned about the conspiracy theories regarding sanitary measures and vaccines against SARS COV2. This denial of fact-based data and diligently curated research takes many forms and is expressed in abundance in social networks in particular. We fear that this article, widely shared on social media,[20] facilitates misinformation and fearmongering around COVID-19 vaccines. Also, the dissemination of false information by physicians on social networks (such as rapid sharing of controversial publications) is a major cause for concern as they are considered a reliable source of guidance for the public, and could lead to suspension or revocation of their medical license.[21] As such, it jeopardizes public health policies and represents a real danger to all of humanity.

The important shortcomings and misusage of scientific literature and data have no place in a scientific journal. Therefore, we suggest that this article should be retracted in an effort to prevent further damages to health care policies.

Words count: 1488 words.

Table 1: Summary of some bibliography misunderstandings

Ref	Quote	Misunderstandings
Liu et al., 2021	"*Vaccination has also been demonstrated to suppress both IRF7 and STAT2*"	This reference only focuses on one non-mRNA vaccine (inactivated SARS-CoV-2 Vaccine (Vero Cell)) and is thus irrelevant to the authors' focus on mRNA vaccines.
Goldman et al., 2021	*"The case study described earlier in this paper strongly supports the hypothesis that these injections induce accelerated lymphoma progression in follicular B-cells"*	A causal link cannot be established based on a single case study as referred to in the quoted article (which reports a case of post-vaccine T angio-immunoblastic lymphoma and not B- follicular NHL). No increase of vaccine induced lymphomas have been reported so far. Anti-SARS-CoV-2 vaccines, on the contrary, are known to be weakly immunogenic in patients with lymphoid hemopathy, especially if they are treated with anti-CD20 monoclonal antibodies.[22]
Karikó et al., 2005)	"*Human cells recognize viral RNA as foreign, and this leads to upregulation of type I IFNs*"	Reference is not specific to viral RNA but describes an upregulation that occurs with "a variety of natural RNAs". The paper is dedicated to the hypothesis "*that nucleoside modification suppresses the immune-stimulatory effect of RNA*" thus giving evidence that could reduce the concerns of the authors when designing future mRNA vaccines. Actually, this paper opposes the author's hypothesis since mRNA vaccines have been designed with pseudo-uridines on purpose.
Forni and Mantovani, 2021	As the authors declared: "*Due to the short development time and the novelty of the technologies adopted, these vaccines will be deployed with several unresolved issues that only the passage of time will permit to clarify*"	The reference mainly emphasizes that "*Technical problems connected with the production of billions of doses and ethical ones connected with the availability of these vaccines also in the poorest countries, are imminent challenges facing us. It is our tenet that in the long run more than one vaccine will be needed to ensure equitable global access, protection of diverse subjects and immunity against viral variants*." In this context, the pledges put forward both by pharmaceutical companies and the director of the US Objective Warp Speed [23] to keep rigorous efficacy and safety standards as an absolutely central issue in COVID-19 vaccine development are reassuring. By not telling which "unresolved issues" are meant in this paper, the reader might be misled by the author's out of context quotation.

Vanderlugt and Miller, 2002	"*These cytokines can induce autoantibody production through epitope spreading*"	The reference is focused on autoimmune and virus-induced immunity with no mention to post-vaccination autoimmunity and is thus irrelevant in the authors' assumptions context. « *Understanding the cellular and molecular basis of epitope spreading in various chronic immune-mediated human diseases [….] is crucial to understanding the pathogenesis of these diseases* » clearly does not refer to mRNA vaccines.
Simone et al., 2021	"*COVID-19 vaccines cause myocarditis and pericarditis, with an increased risk in particular for men below the age of 50*"	No information about pericarditis in the provided reference which is therefore irrelevant to support the authors' claim. "*We evaluated acute myocarditis incidence and clinical outcomes among adults following mRNA vaccination in an integrated health care system in the US*."
Jain et al., 2021	"*COVID-19 vaccines cause myocarditis and pericarditis, with an increased risk in particular for men below the age of 50*"	The study was not intended to identify and/or track pericarditis and was focused on the clinical and imaging characteristics of coronavirus disease 2019 vaccination–associated myocarditis. "*In this study, we aimed to characterize the clinical presentation, short-term prognosis, and myocardial tissue changes as noted on CMR or cardiac MRI in pediatric patients with coronavirus disease 2019 vaccination-associated myocarditis*.»
Choi S et al, 2021 Verma et al., 2021	"*Fatal cases of COVID-19 vaccination have been described*"	Two case reports of death occurring 5 days and 14 days after the first and the second dose of mRNA vaccine. Choi S. et al. conclude that "*The primary cause of death was determined to be myocarditis, causally-associated with the BNT162b2 vaccine* ». Verma et al. mention that "*a direct causal relationship cannot be definitively established.*" Thus, no general conclusions can be drawn from these two cases. No published data support the hypothesis that SARS-CoV-2 vaccines could be a significant cause of fatal issues.
Wei et al.	"*Also, under conditions of overwhelming production of SARS-CoV-2 spike glycoprotein due to SARS-CoV-2 molecular vaccination, it would of course be expected that a significant proportion of over-abundant intracellular spike glycoproteins would also be exported via exosome cargoes*"	The paper mentions that "*exosomes bear specific repertoires of proteins and RNAs, indicating the existence of mechanisms that control the sorting of molecules into them*" which contradicts the author's claim.

No reference	"*Since these vaccines are specifically designed to induce high and ongoing production of SARS-CoV-2 spike glycoproteins, the implications are ominous*."	In a study on 13 healthy volunteers, S1 antigen was detected as early as day 1 postvaccination, and peak levels were detected on average 5 days after the first injection, with no S1 antigen detected at day 10 [24]. Spike protein was detectable in 3 of 13 participants an average of 15 days after the first injection. After the second vaccine dose, no S1 or spike antigen was detectable, and both antigens remained undetectable through day 56. Therefore, the assumption by Seneff et al. is wrong.x

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