Molecular Mimicry between hPF4 and SARS-CoV-2 Spike Protein: Response to Comment

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Semin Thromb Hemost 2023;49:106–107.

To help foster scientific debate, we would like to reply to Mungmunpuntipantip and Wiwanitkit,[1] addressing their perplexities in relation to our previous report.[2] Hafeez et al, in their review of the literature on COVID-19 vaccine-associated thrombosis with thrombocytopenia syndrome (TTS), including 25 articles and 69 patients, reported that "patients having received messenger ribonucleic acid (mRNA) COVID-19 vaccines are also present."[3] They never stated that these vaccines "have also been implicated" as Mungmunpuntipantip and Wiwanitkit concluded.[1] Moreover, Hafeez et al also reported that one of the limitations of their study was the small sample size. In fact, of the 69 patients with vaccine-induced TTS analyzed within the review, only 4 patients had received an mRNA vaccine (5.7%), while the others had received an adenovirus-based vaccine, and no other details regarding their comorbidities was present and no statistical analysis was performed proving the relationship between mRNA COVID-19 vaccines and TTS.

Mungmunpuntipantip and Wiwanitkit[1] also stated in response to our prior report[2] that "there was no data provided on similarity score. Moreover, a comparative genomics analysis can give a similarity score but it cannot provide the statistical level of similarity or difference." We raise several objections to this statement; the first one is that SWISS-Model has not shown any similarity between spike glycoprotein and platelet factor 4 (PF4) since they have very different structures, and since no similarity was found the similarity score could be estimated as approximately 0. The second objection is that the sentence is self-contradictory because it states that a similarity score cannot provide a statistical level of similarity (i.e., a similarity score). The third objection is that we have performed a structural/amino-acidic analysis, not a genomic analysis. In addition, we would like to specify that we have provided all the information necessary to replicate what we have performed. Moreover, Baker et al[4] demonstrated that all three adenoviruses deployed as vaccination vectors bind to PF4, enforcing the hypothesis that TTS is related to viral vector vaccines rather than to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mRNA.

Finally, Mungmunpuntipantip and Wiwanitkit[1] stated that "there are additional means of providing such proof. One good example is using a bioinformatics molecular docking technique to enable prediction of the interaction between two studied molecules." This was not the original aim of our article[2] since we wanted to investigate the possibility of structural similarities and cross-recognition between SARS-CoV-2 spike glycoprotein and PF4 protein (i.e., molecular mimicry); however, following the suggestion of Mungmunpuntipantip and Wiwanitkit,[1] we have also performed molecular docking analysis using RaptorX Web server and no possible statistically significant interaction has been found (the highest aminoacidic interaction probability reached between spike glycoprotein and PF4 reached 50% of probability).[5] Moreover, the aminoacidic positions with the highest interaction probability are in an internal region of spike glycoprotein. In conclusion, we believe that the statements made by Mungmunpuntipantip and Wiwanitkit[1] are contradictory, and do not provide any new evidence or information. On the contrary, McGonagle et al[6] reported in their review that many scientific articles have demonstrated

article published online June 21, 2022

Issue Theme Maintaining Hemostasis and Preventing Thrombosis in COVID-19—Part IV; Guest Editors: Emmanuel J. Favaloro, PhD, FFSc (RCPA), Leonardo Pasalic, FRCPA, FRACP, PhD, and Giuseppe Lippi, MD

Thieme Medical Publishers, Inc., 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA

DOI https://doi.org/10.1055/s-0042-1744280.
ISSN 0094-6176.

our initial hypothesis with different methods and provided much useful information to better understand this terrible virus.

Conflict of Interest
None declared.

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