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

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We would like to share our ideas on the publication "Is Molecular Mimicry between hPF4 and SARS-CoV-2 Spike Protein a Potential Basis for Autoimmune Responses in Vaccinated and Naturally Infected Patients?."[1] Carnevale et al performed a comparative sequence analysis and epitope prediction using bioinformatics techniques and concluded that "These results suggest that probably the molecular mimicry between the hPF4 and the SARS-CoV-2 spike protein is not responsible for the prothrombotic events associated with VITT."[1] There were no statistically significant homologies or similarities in the structures of human platelet factor 4 (hPF4) and spike glycoprotein, according to their report on sequence comparative analysis,[1] and no possibly overlapping B cell epitope was detected. However, no direct examination of the interaction between antibody and virus/PF4 has yet been conducted.[1] A vaccine-related thrombocytopenia with thrombosis condition (vaccine-inducted thrombotic thrombocytopenia [VITT]) has been attributed to use of adenovirus-based COVID-19 vaccines in the majority of cases; however, messenger ribonucleic acid COVID-19 vaccines have also been implicated.[2] Individuals who present with symptoms suggestive of VITT, and who have received a COVID-19 vaccine within the last 4 weeks should be carefully assessed.[2] The prior study by Carnevale et al[1] can provide data on similarity between hPF4 (Reference Sequence: NG032897) and surface spike glycoprotein (Reference Sequence: YP_009724390.1). However, 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. Therefore, how Carnevale et al concluded on "statistically significant homologies or similarities" requires clarification. Regarding epitope predictions, several tools are available, and some can provide a list of possible epitopes.[3] Without data from such prediction models, we also raise questions in regard to how Carnevale et al[1] concluded that "no potentially overlapping B cell epitope was found." Conversely, if there is a region of overlapping, this does not necessarily mean anything in regards to interaction with an antibody, but simply that there are shared common antigenic regions within molecules. Finally, to enable proof of possible interaction, Carnevale et al suggested further performance of "binding experiments with …. both surface plasmon resonance and immunoprecipitation."[1] In fact, 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.[4]

Conflict of Interest
None declared.

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