Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Editorial commentary: The platelet in COVID-19: A critical participant or a bystander?

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Platelets are the smallest blood cells in the human body, yet an essential component for life. For a long time, we thought that platelets' functions were restricted to their role in blood clotting and platelets aggregation. This traditional dogma has been challenged in the last decades and we now realize that platelets are implicated in various pathophysiological conditions including; wound healing, inflammation, carcinogenesis and immune response to viruses[1]. In fact, platelets express hundreds of thousands of receptors on their cell membranes that are important for normal functions. Some of the well-recognized platelets' receptors are integrins, selectins, GPCRs, lipid receptors and immunoglobulin receptors (to name a few)[2]. Many of platelet's receptors are rapidly activated early during infection and accordingly, platelets can be viewed as one of the first line defenses against various pathogens, including viruses[3].

Viruses, in general, initiate their first contact with host cells via viral binding to cell surface receptors. This binding mediates viral internalization through the endocytic pathways, allowing injection of the viral genome into host cells[4]. Interestingly, platelets' receptors have been reported to interact with numerous viruses and to mediate viral entry[5]. Although lacking nuclei, platelets retain part of the protein synthesis machinery and are able to synthesize some proteins from viral RNAs[6]. Recently, the ACE2 receptor was also found on platelets' surfaces and thus, SARS-CoV2 is able to internalize human platelets and directly activate them[7]. This mechanism can provide another explanation of the strong correlation between COVID-19 and coagulopathy. Likewise, this begs the question of what is the exact role of platelets in COVID-19-associated coagulopathy?

In this review, Iba and Levy[8] demonstrated the roles of platelets in COVID-19-associated coagulopathy and vaccine-induced thrombotic thrombocytopenia. The authors thoroughly reviewed a body of recent literature investigating both direct and indirect interactions between SARS-CoV2 and platelets. These interactions are rapidly activating platelets and thus stimulating them to release various thrombotic factors including, platelet factor 4, ADP, von Willebrand factor and P-selectins. In their turn, these factors facilitate platelets aggregation and clot formation in COVID-19. Iba and Levy[8] also emphasized the potential role of platelets in the viral vectored COVID-19 vaccine-induced thrombotic thrombocytopenia. To this end, the authors proposed an intriguing model in which the free DNA from the vaccine binds to the released platelet factor 4. This DNA-platelet factor 4 complex elicits immunogenicity and stimulates anti-platelet factor 4 autoantibodies that contribute to immunothrombosis. Indeed, patients with higher levels of anti-platelet factor 4 antibodies have more incidents of thrombotic events after receiving the viral vectored vaccine[9].

The review by Iba and Levy[8] is important because it demonstrates a potential role of platelets in both COVID-19-associated coagulopathy and vaccine-induced thrombotic thrombocytopenia. The authors should be congratulated as they provide mechanistic models for platelets activation in these conditions and, in theory, this may help to open new avenues in improving COVID-19 outcomes and/or mitigating vaccine-induced immunothrombosis. However, the exact role of platelets in both COVID-19- and viral vectored COVID-19 vaccines-induced thrombosis remains an open question. For example, the mixed results concerning the effectiveness of antiplatelets for COVID-19[10]· [11] make the reader to wonder whether the platelets are critical participants or just bystander players in the pathogenesis of the disease. Likewise, it remains to be answered whether thrombotic events induced by viral vectored COVID-19 vaccines are applicable to all other viral vectored vaccines. Importantly, increasing the safety of these new vaccines will remain an active area of future research.

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