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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Cardiovascular complications in the post-acute COVID-19 syndrome: A novel perspective down the road

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Dear Editor:

The pathogen responsible for the pandemic of the Coronavirus Disease 2019 (COVID-19) is Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). This has resulted in worldwide healthcare crises and strained health resources. As the number of people recovering from COVID-19 rises, it is critical to know the healthcare challenges surrounding them. COVID-19 is now recognized as a multi-organ illness with many symptoms. Increasing reports of persisting and extended sequelae following acute COVID-19 infection, similar to post-acute viral symptoms documented in survivors of past virulent coronavirus outbreaks. Patient advocacy groups, many of whose members identify as long haulers, have contributed to the identification of post-acute COVID-19, a syndrome marked by persistent symptoms and/or delayed or long-term problems beyond 4 weeks after the beginning of symptoms. The mechanism or processes underlying the link between COVID-19 and the development of cardiovascular illnesses in the post-acute phase of the disease are not completely understood [1,2]. A recent study reported that Individuals with COVID-19 are at a higher risk of incident cardiovascular disease after the first 30 days of infection, including cerebrovascular disorders, dysrhythmias, ischemic and non-ischemic heart disease, pericarditis, myocarditis, heart failure, and thromboembolic disease. The authors of this study showed that the risk and 1-year burden of cardiovascular disease in survivors of acute COVID-19 are significant. In this regard, the findings of this study highlighted the importance of improving strategies for primary prevention of SARS-CoV-2 infections; that is, the best way to avoid Long COVID and its numerous complications including the risk of cardiovascular severe complications. Further, given the large and growing number of people with COVID-19 (more than 570 million globally), the risks and 12-month burdens of cardiovascular diseases confirmed in the previous study could potentially affect a large number of people worldwide [3]. Therefore, cardiovascular health and illness should be addressed in the care pathways of people who survive with an acute episode of COVID-19. Besides, long-term studies on the SARS-CoV-2 infection are needed to understand the effects on atherosclerosis and the function of prophylactic treatments. Here, we would like to shed light on a potential mechanism that may be responsible for cardiovascular complications in persons who survive after an acute episode of COVID-19. The COVID19 has been linked to systemic inflammation, a "cytokine storm," hemostasis changes, and severe vasculitis, with accumulating data suggesting that dysregulation of lipid transport may play a role in some of these consequences. Hence, researchers proposed that changes in the amount and content of High Density Lipoprotein (HDL) caused by COVID19 might drastically reduce HDL's anti-inflammatory and antioxidant activities, thereby contributing to virus-associated organ inflammation. In the context of COVID19, it was recently shown that a low level of HDL is related to disease severity and death. HDL is a diverse group of particles with varying sizes and apolipoprotein compositions. The predominant protein ingredient of HDL is Apolipoprotein AI (ApoAI), found in most HDL particles. However, other apolipoproteins, such as Apolipoprotein E (ApoE), are connected with certain HDL particle subtypes. The interaction between particularly lipid-poor ApoAI in tiny discoidal (prebeta) forms of HDL and cell-bound transporters such as ATP-Binding Cassette Transporter (ABCA1) and ATP Binding Cassette Subfamily G Member 1 (ABCG1), drives cellular cholesterol efflux, the first step in Reverse-Cholesterol Transport (RCT) from the periphery to liver [4]. Clinically, poor HDL function or RCT leads to cardiovascular disease [4]. ABCA1 and ABCG1 in macrophages enhance RCT in vivo, and their actions are cumulative [5]. Another study discovered that the ABCG1 route, not the ABCA1 pathway, was linked to the reduction in coronary lipid load. ABCG1-mediated cholesterol efflux was advantageous in individuals with more unstable clinical presentations of coronary plaques [6]. ABCG1 is a transmembrane cholesterol transporter that transports cellular cholesterol from macrophages to mature HDL particles. A

Abbreviations: COVID-19, Coronavirus Disease 2019; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; HDL, High Density Lipoprotein; ApoAI, Apolipoprotein AI; ApoE, Apolipoprotein E; ABCA1, ATP-Binding Cassette Transporter; ABCG1, ATP Binding Cassette Subfamily G Member 1; RCT, Reverse Cholesterol Transport.

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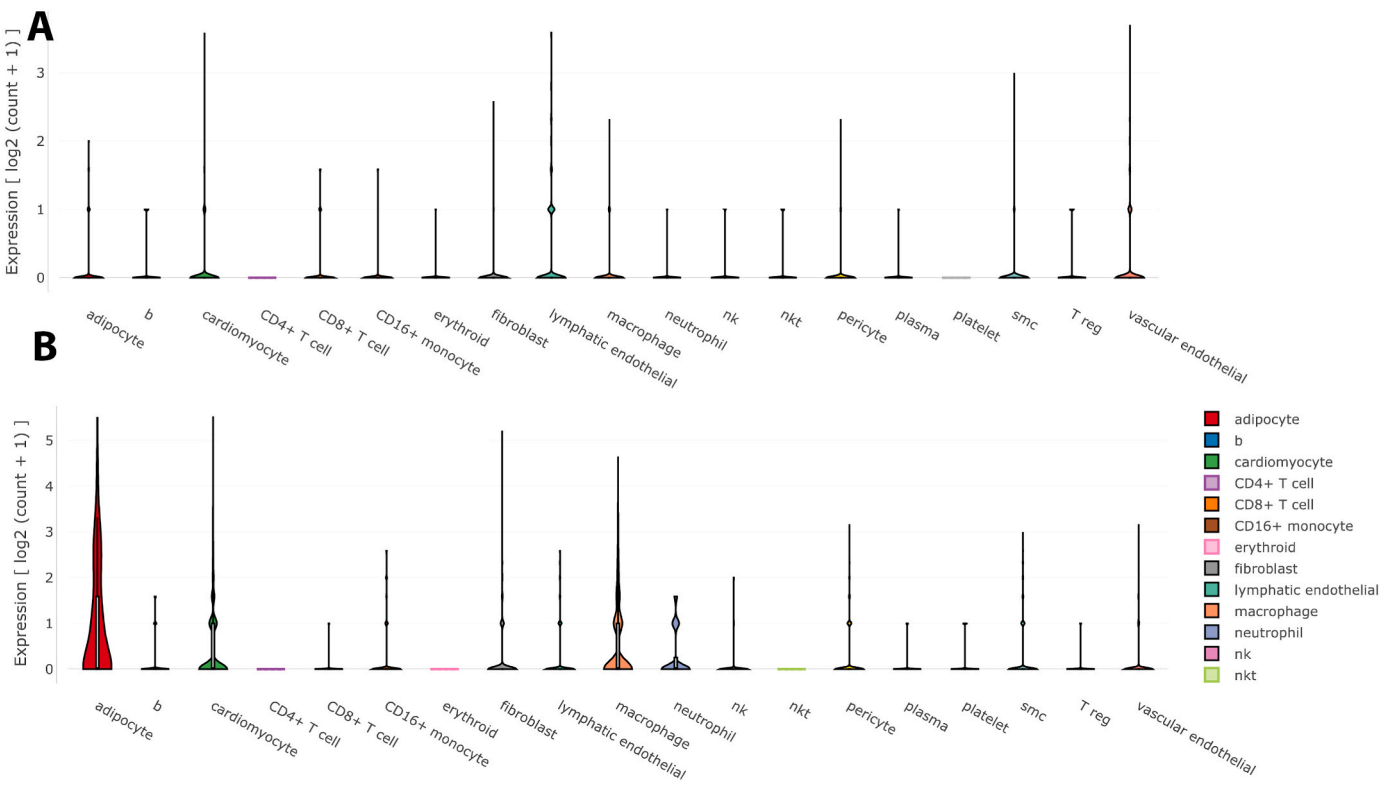

Fig. 1. ABCG1 (A) and ABCA1 (B) expressions in distinct immune cells based on single-cell transcriptomics analysis of COVID-19 heart autopsy data.

functional variant in ABCG1 is associated with an increased risk of myocardial infarction and ischemic heart disease in the general population [7]. To uncover pathologies and cellular targets of SARS-CoV-2 related to ABCA1 and ABCG1; we used data from 40,880 single-cell nuclei were taken from the hearts of 18 SARS-CoV-2 infected COVID-19 autopsy donors [8]. Our findings show that ABCG1 is not expressed in macrophages or other immune cells (Fig. 1A). Furthermore, compared to other immune cells, such as adipocytes, our investigation revealed that macrophages have low expression of ABCA1 (Fig. 1B). As a result, we may conclude that ABCG1 depletion in macrophages is responsible for post-acute COVID19 cardiovascular problems because of impaired HDL and RCT functions.

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