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Wnt5a and Wnt11 as acute respiratory distress syndrome biomarkers for severe acute respiratory syndrome coronavirus 2 patients

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To the Editor:

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has spread globally, resulting in declaration of pandemic emergency [1]. COVID-19 patients suffer from various symptoms of infection, including pneumonia, acute respiratory distress syndrome (ARDS) and sepsis. Some known antiviral drugs, including remdesivir, have been proposed as effective agents for the treatment of SARS-CoV-2 infection [2, 3]. Along with the development of potential therapeutics, there is urgency to mitigate the transmission and economic crisis of SARS-CoV-2 *via* identification of biomarkers that can rapidly indicate the severity of the disease in infected patients. Wnt ligands are secreted glycoproteins and their downstream signalling plays a pivotal role in embryonic development and tissue homeostasis. With remarkable progress in the immunology field, Wnt signalling has gained much attention as a critical regulator in various inflammatory diseases. A large body of evidence has suggested that Wnt ligands are secreted by immune cells, such as peripheral blood mononuclear cells (PBMCs) and non-immune cells, including stroma cells, to regulate inflammatory

response and immune cell modulation [4–7]. In addition to their roles in inflammation, studies have reported that these Wnt ligands play key roles in tissue damage and repair [6]. Interestingly, prior studies have reported significant alterations in Wnt5a and Wnt11 expression compared to other Wnt ligands by analysing sera of patients with severe sepsis or sepsis mouse models [4, 8]. Wnt5a signalling has been known to activate in sepsis or ARDS and play a pivotal role in lung inflammation and fibrosis [5, 9], whereas Wnt11 protein has been reported to suppress induction of inflammatory cytokines by regulating NF-κB activity [10, 11]. Previous reports have demonstrated that Wnt5a and Wnt11 have opposite functions to one another in response to inflammation [12, 13]; hence it is thought that Wnt5a has pro-inflammatory effect and Wnt11 may be anti-inflammatory. Therefore, we focused on Wnt5a and Wnt11 to explore their potential relevance to COVID-19-related diseases. In this study, we report Wnt5a and Wnt11 as reliable biomarkers for monitoring of pathological progression in SARS-CoV-2 patients.