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Association Between Host Gut Microbiota and SARS-CoV-2 Infection

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Dear Editor,

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel coronavirus that causes coronavirus disease 2019 (COVID-19). Since its emergence in December 2019, it has infected millions of people around the world. On January 30, 2020, the epidemic was announced as the Public Health Emergency of International Concern by the World Health Organization.[1] Although the majority of studies have concentrated on respiratory symptoms findings, the potential role of gut microbiota in the development of the clinical features of COVID-19 has been documented as well.[1]

It has been proven that the highest mortality of SARS-CoV-2 is among the elderly and patients with underlying health disorders such as diabetes. Interestingly, these patients have less diverse gut microbiomes.[2] According to reports, an association exists between shifts in the gut microbiome and age-related health decline.[2] A shift from *Firmicutes* toward genera such as *Alistipes* and *Parabacteroides* has been described in the elderly gut microbiome. There are also documents of microbiome shifts in asthmatic and diabetic patients.[2] A reduction of the phylum Bacteroidetes while an abundance of *Bifidobacteria* happens in chronic obstructive airway disease and type-II diabetic patients, respectively.[2] In addition, evidence indicates that the lung microbiome among COVID-19 patients changes and the attendance and increase of gut microbiota in the lungs of patients are associated with the onset of acute respiratory distress syndrome (ARDS) and elevated levels of inflammatory markers in plasma. ARDS is a common complication in severe cases of COVID-19, and documents show that the lung microbiota differs in patients with and without ARDS. Therefore, the alteration of the microbial composition of the lungs of COVID-19 patients can be a tool for predicting the occurrence of ARDS.[3] The findings of a study based on the sequencing technique revealed that intestinal *Bacteroides* species were present in 41% of patients compared to 3.8% of healthy individuals. The results of another study demonstrated that the rate of intestinal Enterobacteriaceae spp. in patients with severe ARDS increased compared to other patients.[1] The change in the gut flora caused by SARS-CoV-2 can be related to the physiological functions of the main target of this virus, namely, angiotensin-converting enzyme 2 (ACE2). ACE2 is a surface protein of intestinal epithelial cells that regulates tryptophan uptake, and the mentioned amino acid also regulates the expression of antimicrobial peptides. Furthermore, molecular studies suggest that ACE2 expression is downregulated during infection in COVID-19 patients. As a result, ACE2 downregulation reduces the intestinal uptake of tryptophan and decreased expression of antimicrobial peptides, ultimately, leading to increased intestinal pathogens and gut dysbiosis.[4] It has also been shown that part of the effect of the microbiome on COVID-19 can be related to the impacts of the microbiome on cytokine secretion. More interestingly, the production of cytokines is strongly influenced by microbial metabolic pathways in the gut. Considering that the occurrence of some severe clinical cases of COVID-19 disease such as acute respiratory distress syndrome (SARDS) or multi-organ failure is due to hyperinflammation and excessive levels of cytokines release, the intestinal microbial composition may play a decisive role in the clinical outcome of COVID-19 patients.

Finally, due to the important role of gut microbiome changes in the development of SARS-CoV-2 infection, a detailed understanding of these changes allows the development of effective treatments for this novel disease. Additionally, the presence of gut microbiota in the lungs of COVID-19 patients can be a predictor of ARDS. Accordingly, knowing about the host and microbiota molecular pathways associated with cytokine responses

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may provide microbiome-based therapeutic approaches for COVID-19.

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