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LETTER TO THE EDITOR

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Gut dysbiosis and long COVID-19: Feeling gutted

To the Editor,

COVID-19 is primarily a respiratory illness, however, there is compelling evidence proposing a lung-gut axis involved in the disease. We explored emerging evidence suggesting a possible link between dysbiosis of the gut microbiota and long-term complications from COVID-19.

Emerging evidence has suggested that the pathology of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may in part be explained by microbial species,[1] contributing to the inflammatory phenotype commonly seen in patients with coronavirus disease (COVID-19).[2,3] Indeed, dysbiosis of the gut microbiota has been associated with poor clinical outcomes in mechanically ventilated COVID-19 patients. Specifically, Wu *et al.* observed elevated *Granulicatella* and *Rothia mucilaginosa* in the gut microbiome of COVID-19 hospitalized patients when compared to healthy individuals.[4] Additionally, increased *Burkholderia cepacia complex*, *Staphylococcus epidermidis*, *Mycoplasma hominis*, and *Mycroplasma orale* species have been observed in severely ill COVID-19 patients as opposed to mildly affected ones.[5] These findings hint at a possible yet prominent link between gut microbiota and SARS-CoV-2 repercussions, which may also be related to the imminent occurrence of long-term COVID-19 complications.

Contemporary research has revealed a disruption of the gut microbiota in stool samples of SARS-CoV-2 patients that may explain the well-described cytokine storm-induced ramifications post-infection.[6] Interestingly, fecal transplantation may regenerate gut microbiota diversity, bolstering the respiratory system of patients suffering from COVID-19.[7] Considering that long-term complications following recovery from SARS-CoV-2 persistently exhibit a damaged microbial microenvironment compared to uninfected controls,[8] these changes may hint at alterations in the patients' microbiome. We describe recently published data on the relationship of the long COVID-19 phenomenon with gut microbiota dysbiosis, providing a mechanistic insight. Our aim is to raise awareness of the impact SARS-CoV-2 imposes on public health that in part may be explained through a gut-lung axis cascade.

The depletion of immunomodulatory microbiota from severe SARS-CoV-2 infection may prolong physiological repercussions (i.e., lung injury) during long COVID-19, induced by systemic inflammation.[9] The recent study by Chen *et al.* showed significant reductions of microbial diversity in patients with COVID-19 during a 6-month follow-up, as opposed to the aseptic group.[10] Particularly, following acute (30 days) and prolonged (3 months)

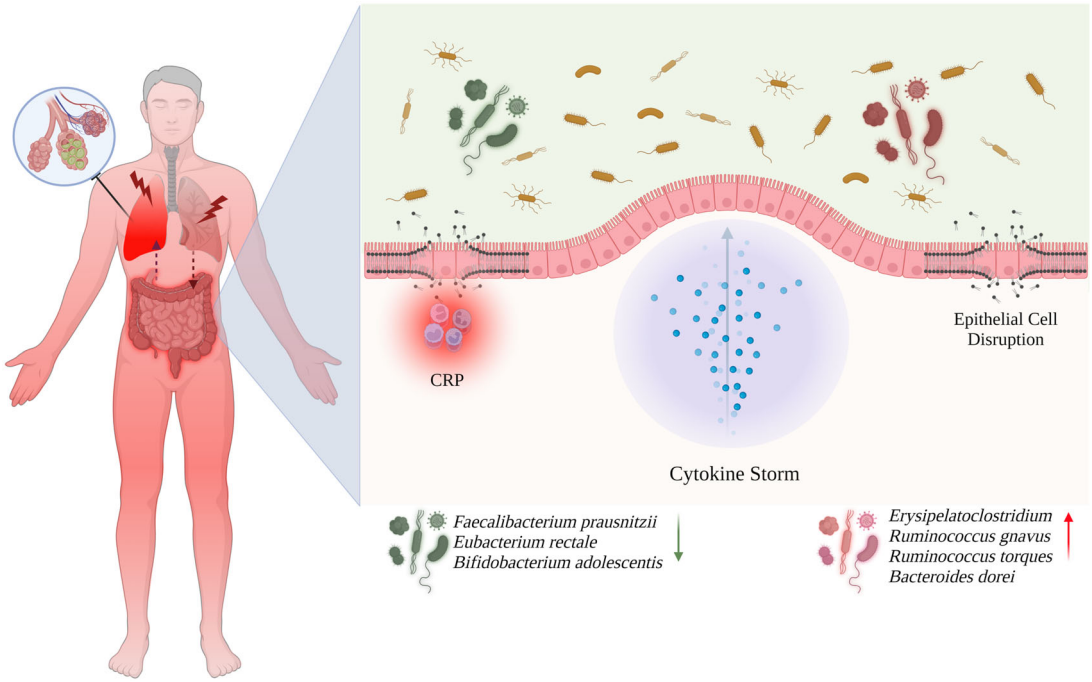

FIGURE 1 Lung–gut axis microbial dysbiosis in long SARS-CoV-2. CRP, C-reactive protein

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SARS-CoV-2 recovery, suppression of anti-inflammatory bacteria such as *Faecalibacterium prausnitzii*, *Eubacterium rectale*, and *Bifidobacterium adolescentis*, and enrichment of pathogens, including *Rothia*, *Erysipelatoclostridium*, *Ruminococcus gnavus*, *Ruminococcus torques*, and *Bacteroides dorei* have been observed.[8,11] These changes may underlie the association between lower gut microbiota diversity and higher C-reactive protein levels in long COVID-19 patients (Figure 1).

The substantial increase of pathogenic bacteria concomitantly with decreased anti-inflammatory microbiota, advocates for a prominent link between sustained intestinal inflammation during COVID-19 infection. Therefore, these alterations may subsequently lead to prolonged SARS-CoV-2 recovery, campaigning for the importance of a favorable gut microenvironment. Clinical trials experimenting with supplementation of anti-inflammatory bacterial species and/or fecal transplantation may be imperative to accelerate gut microbiota restoration and long COVID-19 rehabilitation.

AUTHOR CONTRIBUTIONS

Panagiotis Giannos made an investigation plan and drafted the manuscript. Konstantinos Prokopidis conceived the idea and revised the manuscript critically for important intellectual content.

CONFLICTS OF INTEREST

The authors declare the absence of any commercial or financial relationships that could be construed as a potential conflicts of interest.

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