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.

Reply. We would like thank Drs Tursi and Papa for their interest and positive comments on our study. Their comments reinforced the crucial role of the gut-lung axis in the pathogenesis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and provided further evidence to support modulation of the gut microbiota as an adjunctive therapy for coronavirus disease 2019 (COVID-19).[1]

A recent study that analyzed the stool samples of more than 100 patients with COVID-19 reported that individuals with lower levels of beneficial bacteria species had higher levels of inflammatory cytokines, suggesting a link between an individual's gut microbiome composition and severity of the SARS-CoV-2 infection.[2] It has also been found that altered gut microbiome composition persists after recovery and may contribute to lingering symptoms, known as "long COVID."[3] These data are a strong impetus for consideration of microbiota modulation to facilitate timely recovery and reduce the burden of postacute COVID-19 syndrome.

While how the gut microbiome influences the health of its host it is not yet fully understood, one mechanism is thought to be through substances known as metabolites that bacteria release. These metabolites themselves can reach other organs and tissues and appear to have a significant influence on the immune system. A recent study reported that patients with COVID-19 displayed impaired capacity for short-chain fatty acid and L-isoleucine biosynthesis in their gut microbiome that persisted after recovery and correlated with disease severity and host immune responses. These findings suggest that strategies to supplement short-chain fatty acid or L-isoleucine could be developed to improve disease outcome.[4]

Tursi and Papa highlighted the role of high-dose probiotics in improving outcomes in patients hospitalized with COVID-19. Our recent data[5] supported this concept. In an open-label pilot study, we recently tested the efficacy of a newly developed probiotic formula (SIM01), which is an oral encapsulated formulation of 3 lyophilized *Bifidobacteria* and 3 prebiotics, as an adjuvant therapy on immunologic response and gut microbiota among patients hospitalized for COVID-19. Interestingly, we found that individuals with COVID-19 who were given SIM01 had hastened antibody formation against SARS-CoV-2, reduced plasma proinflammatory markers, and showed a reduction in nasopharyngeal viral load compared with a control group. Using metagenomic sequencing, we demonstrated colonization of the bacterial species in SIM01, which was associated with restoration of gut dysbiosis associated with SARS-CoV-2.[5]

Recent evidence suggests that the gut microbiota is involved in the humoral immune response and could shape the B-cell repertoire after vaccination.[6] It has been reported that differential baseline bacterial species were associated with higher vaccine response. Specifically, the presence of an immunomodulatory bacteria, *Bifidobacterium adolescentis*, was associated with higher neutralizing antibodies to CoronaVac (Sinovac Biotech Ltd, Beijing, P.R. China), suggesting that this bacteria may serve as an adjuvant to potentially overcome waning immunity of inactivated vaccine.[7] Although the BNT162b2 vaccine induced more than 90% neutralizing antibody response, waning of spike-antibody levels has been reported in infection-naïve individuals over a period of 3 to 10 weeks after the second vaccine dose.[8] Further investigation on the longitudinal assessment of the gut microbiota profile and antibody response in the longer term will have significant implications in delineating how microbiota influences immunogenicity and long-term durability of vaccine response.

In summary, the therapeutic rationale of the modulation of the intestinal microbiota as adjunctive therapy for COVID-19 is likely to be applicable not only to improved outcome in patients with COVID-19 but also to improve vaccine response and reduce vaccine-related adverse effects. Well-designed clinical trials will be important to advance our knowledge on the potential of gut microbiota manipulation as an adjuvant therapy for SARS-CoV-2 infection and immunization schedule.

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Conflicts of interest
The authors disclose the following: Francis K.L. Chan and Siew C. Ng are the scientific co-founders of GenieBiome Ltd, and the Chinese University of Hong Kong hold a provisional patent for A Synbiotic Composition for Immunity.

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https://doi.org/10.1053/j.gastro.2022.02.022