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Mechanistic studies are also needed to confirm the functions of beneficial gut commensals and to exploit these microorganisms for therapy.

TAO ZUO

YUN KIT YEOH

SIEW C. NG

Center for Gut Microbiota Research  
The Chinese University of Hong Kong  
Hong Kong, China *and*  
Department of Medicine and Therapeutics  
LKS Institute of Health Science  
The Chinese University of Hong Kong  
Hong Kong, China

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### Conflicts of interest

The authors disclose no conflicts.

### Most current article

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## Dysbiosis in SARS-CoV-2-Infected Patients



To the Editors:

Gastrointestinal symptoms are frequently observed in patients with coronavirus disease 2019 (COVID-19), but only limited knowledge is available regarding the ability of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to influence the host microbiota composition. The entry of SARS-CoV-2 into intestinal cells down-regulates angiotensin-converting 2 receptors and causes microbial dysbiosis.<sup>1,2</sup> An alteration of the microbial composition may impact the pulmonary defense mechanisms through the so-called gut–lung axis.<sup>3</sup> We have read with interest the articles by Zuo et al<sup>4</sup> confirming the impact of COVID-19 on the gastrointestinal tract’s microbial community composition. Remarkably, their article represents, to our knowledge, the first publication exploring the complex association between SARS-CoV-2 infection and fungi, a neglected component of the gut microbiota. Gut bacteria inhibit the growth of *Candida albicans* and other gut fungi via the target of rapamycin signaling pathway and through those tryptophan metabolites, which are responsible for an interleukin-22-dependent mucosal

response.<sup>5,6</sup> Bacteria and fungi compete for some nutrients and, in this context, bacteria with probiotic properties may control *Candida* overgrowth. In healthy volunteers, a commercially available probiotic product has induced a significant fecal anti-*Candida* activity associated with the augmented production of interferon-alfa in the gastrointestinal tract.<sup>7</sup> Another probiotic formulation administered to patients with COVID-19 has induced a significantly faster remission of gastrointestinal symptoms and other symptoms, such as fever, cough, dyspnea, headache, myalgia, and a decreased risk of evolving respiratory failure compared with nontreated patients.<sup>8</sup> These preliminary data should encourage the scientific community to investigate the possible use of probiotics in patients with COVID-19, keeping in mind that not all probiotic formulations are equivalent for efficacy and safety in these fragile patients.

MASSIMILIANO MARAZZATO

GIANCARLO CECCARELLI

GABRIELLA D’ETTORRE

Department of Public Health and Infectious Diseases  
University of Rome  
Sapienza, Italy

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**Reply.** We are grateful for the interest of Marazzato and colleagues in our article and we would like to take the opportunity to respond to their interesting comments. We agree that intestinal dysbiosis is likely to have a long-reaching impact on the pulmonary immune defense system, and hence might be a risk for respiratory distress or other complications induced by coronavirus disease 2019 (COVID-19).<sup>1</sup> Besides differences in fecal mycobiome composition elucidated in the current article,<sup>2</sup> we have also shown that patients with COVID-19 had altered fecal bacterial microbiome characterized by enrichment of opportunistic pathogens and depletion of beneficial commensals, including short-chain fatty acid producing bacteria.<sup>3</sup> The latter was negatively associated