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## Letter to the Editor

# Will COVID-19 Infection be Less Severe in Ulcerative Colitis Than in Crohn's Patients, Due to a Lower Rate of Smokers?

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Accumulating evidence indicates that smoking history is a poor prognostic factor in patients infected with COVID-19. Virus entry and activity are primarily related to the angiotensin-converting enzyme-2 [ACE2] receptor, which provides a human cell-binding site for the S protein of SARS-coronavirus [SARS-CoV], NL63-coronavirus, and SARS-CoV-2.<sup>1</sup> ACE2 is physiologically expressed by lung alveolar epithelial cells and plays an important regulatory role. The engagement between the virus and ACE2 appears to be associated with a dysregulation of ACE2, and could lead to acute lung injury. Smoking upregulates the ACE2 receptor,<sup>1</sup> probably explaining why these individuals are more susceptible to coronavirus infection.<sup>2</sup> Similarly, an elegant study demonstrated that the expression of the MERS-CoV receptor, dipeptidyl peptidase IV [DPP4], was upregulated in the lungs of smokers and chronic obstructive pulmonary disease patients, providing further data in favour of this theory.<sup>2</sup>

Importantly, there are well-known opposing effects of smoking in ulcerative colitis [UC] and Crohn's disease [CD]. Indeed smoking has been demonstrated to be protective in UC, whereas in CD it has been shown to be associated with a more severe course. In line with previous reports, the percentage of active smokers was higher in CD than in UC patients [3.5% versus 2%, respectively] in the Wuhan inflammatory bowel disease [IBD] registry.<sup>3</sup> This difference partly explains why the overall mortality is slightly increased in CD patients with lung cancer or chronic obstructive pulmonary disease [pooled standardised mortality ratio: (1.39, 95% confidence interval [CI]:1.30–1.50).<sup>4</sup>

In a recent article by An and colleagues<sup>3</sup> on the measures adopted by the Wuhan IBD centre to prevent the spread of the new coronavirus [SARS-CoV-2], none of the 318 registered IBD patients reported COVID-19 infection.<sup>3</sup> More recently, in an Italian retrospective cohort study, no IBD patient was diagnosed with COVID-19 but smoking status was not assessed.<sup>5</sup> Based on these findings, we hypothesise that COVID-19 infection may be less severe in the overall population of UC patients than in those with CD, due to a lower rate of smokers. Ongoing large national and international registries on IBD patients infected with COVID-19 are needed to test this hypothesis and clarify the potential role of smoking in this patient population.

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#### **Conflict of Interest**

LPB: personal fees from AbbVie, Janssen, Genentech, Ferring, Tillots, Pharmacosmos, Celltrion, Takeda, Boerhinger Ingelheim, Pfizer, Index Pharmaceuticals, Sandoz, Celgene, Biogen, Samsung Bioepis, Alma, Sterna, Nestle, Enterome, Allergan, MSD, Roche, Arena, Gilead, Hikma, Amgen, BMS, Vifor, Norgine; Mylan, Lilly, Fresenius Kabi, Oppilan Pharma, Sublimity Therapeutics, Applied Molecular Transport, OSE Immunotherapeutics, Enthera, Theravance; grants from Abbvie, MSD, Takeda; stock-options CTMA.

### **Author's Contributions**

CPB and FD wrote the letter. LPB conceived the letter and critically reviewed the content of the paper. All authors discussed the results and contributed to the final manuscript.

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