Olfactory Loss of Function as a Possible Symptom of COVID-19

To the Editor Eliezer and colleagues reported a case where the main symptom expressed by the patient infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was the sudden and complete loss of the olfactory function without nasal obstruction. Computed tomographic and magnetic resonance imaging of the nasal cavity showed bilateral inflammatory obstruction of the patient’s olfactory clefts. We recognize that this approach should reveal important aspects about the possible association between coronavirus disease 2019 (COVID-19) and the loss of smell. We were, however, confused by the rationale used to explain the possible causes of olfactory function loss observed in this patient. Particularly unclear is the raised hypothesis that the olfactory receptor family, a large G protein-coupled receptor family encoded by OR/OLFR genes, could be involved. The authors mention that olfactory receptors are expressed in cortical central neurons, vascular smooth muscle, upper and lower epithelium, and that because SARS-CoV-2 infects the human respiratory epithelial cells through an impairment of the angiotensin-converting enzyme 2 (ACE2) receptor, they believe that this olfactory receptor family could also be selectively impaired.1

The ability to smell relies on the activation of olfactory receptors expressed by the olfactory sensory neurons of the olfactory epithelium.2 Ectopic expression of odorant receptors in nonolfactory tissues has indeed been extensively reported, suggesting unusual roles for these receptors; but there is no evidence so far that they are related to the sense of smell, SARS-CoV-2 infection, or ACE2 function. Therefore, there is no reason to believe that ectopic expression of olfactory receptors provides explanation for the smell loss symptom reported in patients infected with SARS-CoV-2. Recently, more than 1 study3,4 has traced ACE2 gene expression in human olfactory epithelium to supporting cells (sustentacular cells [SUS]) and some basal progenitor cells, but not to olfactory sensory neurons. It is therefore possible that SARS-CoV-2 infects the epithelium through the most apical SUS cells, promoting cell damage and local inflammatory reaction, which can be traced by image scans. At this moment, there is no plausible evidence or mechanisms that implicate olfactory receptors in the pathogenesis of COVID-19.

Bettina Malnic, PhD
Isaías Glezer, PhD

Author Affiliations: Department of Biochemistry, Institute of Chemistry, University of São Paulo, Brazil (Malnic); Department of Biochemistry, Escola Paulista de Medicina, Federal University of São Paulo, São Paulo, Brazil (Glezer).

Corresponding Author: Bettina Malnic, PhD, Av Prof Lineu Prestes, 748, CEP 05508-000, São Paulo, Brazil (bmalnic@iq.usp.br).

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