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Elevated ACE-2 expression in the olfactory neuroepithelium: implications for anosmia and upper respiratory SARS-CoV-2 entry and replicationM. CHEN ET AL.RESEARCH LETTERElevated ACE2 expression in the olfactory neuroepithelium

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*To the Editor*:

The ongoing outbreak of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a major threat to global health [1]. The mechanism of cellular entry by SARS-CoV-2 is through binding to angiotensin-converting enzyme 2 (ACE-2) [2, 3], a metalloproteinase ectoenzyme that primarily functions in the regulation of angiotensin II, but also has non-catalytic roles such as intestinal neutral amino acid transport. The level of ACE-2 protein and its subcellular localisation in the respiratory tract may be a key determinant of susceptibility to infection, symptoms and outcomes in COVID-19. In humans, ACE-2 protein is broadly expressed in the lung, kidney and small intestine [4]. Pathological analysis of COVID-19 *post mortem* samples shows substantial damage in the lung [5], suggesting that the airway is the principal entry and target of SARS-CoV-2. However, analysis of multiple single cell RNA-seq datasets reveal overall low ACE-2 RNA transcription in nasal airway epithelium, with further reduced expression in lower airway club cells and rare expression in alveolar epithelial cells [6]. This pattern of ACE-2 expression provides evidence that the upper, rather than the lower, airway is the initial site of SARS-CoV-2 infection.