Genetically proxied interleukin-6 receptor inhibition: opposing associations with COVID-19 and pneumonia

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To the Editor:

The inflammatory cytokine interleukin-6 (IL-6) is central to orchestrating the immune system [1]. The pathophysiological process underlying severe coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2, consists of an exaggerated host immune response and elevated circulating levels of inflammatory cytokines, including IL-6 [2, 3]. As such, immunomodulatory agents are being investigated for the treatment of COVID-19. Glucocorticoids may limit inflammation-mediated lung injury in patients with severe COVID-19, and consequently reduce progression to respiratory failure and death. The RECOVERY trial found that administration of dexamethasone resulted in lower 28-day mortality among hospitalised COVID-19 patients who were receiving either invasive mechanical ventilation or oxygen alone at randomisation, but not among those who were not receiving any respiratory support [4]. IL-6 receptor (IL6R) inhibition may represent another potential immunomodulatory strategy for treating COVID-19 [5, 6], and a recent meta-analysis of mean IL-6 concentrations demonstrated 2.9-fold higher levels in patients with complicated COVID-19 compared with patients with non-complicated disease [7].