Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Closing the portal to SARS-CoV-2 cellular entry: *May open newer avenues…*

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Dear Editor,

Amidst the wide range of challenges posed by COVID-19 associated thrombosis, the Kumar et al proposition of severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) cellular entry based angiotensin converting enzyme 2 (ACE2) signalling alterations being at the cornerstone of endothelial dysfunction and vascular pro-thrombotic environment, can have potentially important therapeutic implications [1,2]. Taking account of their molecular level description, we wish to highlight a few points to substantiate the clinical perspective of the discussion.

(i) Akin to Kumar and colleagues, the essential role of transmembrane protease serine 2 (TMPRSS2) co-expression in mediating the SARS-CoV-2 cellular entry, has captivated the attention of the fraternity [3–6].
(ii) In this context, the TMPRSS2 inhibitors such as camostat mesylate (CM) and nafamostat mesylate (NM) are being currently envisaged as promising repurposed drugs (approved for treating pancreatitis in Japan) in COVID-19 for their anti-inflammatory and antiviral properties owing to serine protease inhibition and resultant viral cellular entry block [3–6]. A few researchers cite an incremental value to the therapeutic inclusion of a critical host factor blocker like TMPRSS2 inhibitor over an isolated antiviral regimen, in conferring a subsequent resilience to the rapidly developing viral resistance. They opine that the isolated viral point mutations are unlikely to accommodate for such a critical host component block [7].
(iii) A recent retrospective observational case-series by Hofmann-Winkler et al outlined an attenuation of the COVID-19 disease severity marked by lower sepsis-related organ failure assessment (SOFA) scores paralleled by an ameliorated inflammatory profile in the six ICU patients who received CM compared to the five ICU patients treated with hydroxychloroquine [3]. The maximum CM dose administered in their evaluation amounted to 2 × 100 mg pills three times daily for 5 days which was in accordance with the protocol of a large Denmark randomized controlled trial (RCT, CamoCo-19, NCT04321096). In addition to the aforementioned, a number of double to quadruple blinded RCTs are also ongoing with the aim of evaluating the role of CM as a monotherapy or as an add-on therapy in COVID-19 patients [4].
(iv) Centralizing the focus on thrombosis as in Kumar et al discussion [1], NM has additional anticoagulant and antifibrinolytic effects with Asakura and Ogawa suggesting a heparin and NM combination therapy in COVID-19 patients [5,6]. Interestingly, three elderly high-risk SARS-CoV-2 pneumonia patients with a progressive disease despite antiviral therapy demonstrated an improved clinical profile following administration of 200 mg NM over a span of 24 h [6].

To conclude, the therapeutic armamentarium against COVID-19 is doubtlessly going to become more SARS-CoV-2 specific as an augmented comprehension of the disease related mechanisms transpires. This is heralded by the exemplar of a comprehensive SARS-CoV-2 cellular level patho-physiological description staged by Kumar et al [1], in opening distinctly novel and selective therapeutic avenues aimed at the highest priority societal goal of mitigating the COVID-19 associated morbidity and mortality.

CRediT authorship contribution statement

Ridhima Sharma: Conceptualization, Writing - original draft. **:** . **Rohan Magoon:** Conceptualization, Writing - original draft, Conceptualization, Writing - original draft. **Brajesh Kaushal:** Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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