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Treatments for COVID-19: emerging drugs against the coronavirus

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To the Editor,

With great interest, we read a recent article entitled "Treatments for COVID-19: emerging drugs against the coronavirus" (1). We want to congratulate the authors on their well-structured review highlighting current major investigational agents for coronavirus disease of 2019 (COVID-19) treatment. The graphic summary of emerging drugs provided an overall view of current agents and their targets. Despite the main pharmacological strategies described thoroughly by the authors, we believe that exocytosis and the spread of the infection are overlooked.

Although the exact mechanism of this process is not fully understood in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) yet, it is highly probable that the SARS-CoV-1 and 2 use the same cellular infrastructure given the almost 80 % similarity in sequence identity between SARS-CoV-1 and 2 (2). SARS-CoV-1 is dependent on close interaction with the reticulovesicular network for exocytosis, mainly through the Golgi system. This interaction is assumed to be associated with the Golgi coatomer complex. The complex is part of the coating for nonclathrin-coated vesicles and plays an essential role in vesicular trafficking and budding. The coatomer protein (COP) complex contains seven protein subunits, including coatomer protein complex subunit beta2 (COPB2). Wilde et al. reported that cells with defective COPB2 subunits have significantly reduced protein expression of SARS-CoV-1 and a >2-log decrease in virus yield (3).

In 2020 aiming to find an anti-SARS-CoV-2 treatment among existing medications, the Library of Integrated Network-based Cellular Signatures (LINCS) L1000 database was screened by artificial intelligence based on gene expression mediated by approved or investigational drugs. COPB2 gene expression is essential in the replication of SARS-CoV-1. Subsequently, molecules with gene expression signature that resemble the effects of COPB2 gene knock out are expected to have anti-SARS effects. Authors found reserpine causing the change in gene expression similar to COBP2 gene knockout, so they concluded that reserpine might be a potential agent against COVID-19 (4). Results were consistent with Wu et al. reports in 2004 that identified reserpine the second top compound among 10,000 agents, based on their in vitro activity against SARS-CoV-1 (5).

Duarte et al. reported reserpine as the most effective compound in reversing the transcriptional signature in carcinoma human alveolar basal epithelial cells (A549), which was infected by SARS-CoV-2 (2).

In conclusion, we wanted to suggest reserpine, a known antihypertensive medication found in some members of the genus *Rauwolfia* (5). These findings make reserpine an up-and-coming potential agent for treating COVID-19. We would like to urge the scientific community to explore this in future designated trials. Such efforts will lead to a better chance of finding the solution to this catastrophic global concern.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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