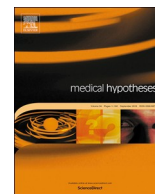




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## Letter to Editors

## Suggesting Ritonavir against COVID-19/SARS-CoV-2



To the Editor,

The novel coronavirus (SARS-CoV-2) has now spread across the globe, affected over 2475723 people, and killed 169151 (as of 21 April 2020). Today, the disease caused by the virus, named COVID-19, has created havoc, a health emergency, and burden on healthcare and global economy. The world is now facing acute crisis of manpower and resources. COVID-19 affects people of all ages, however the fatality was found to be more in people with immunodeficiency and/or chronic illness. The symptoms of COVID-19 range from mild cold to severe pneumonia, often requiring life support systems. Structural biology approaches have determined 3-dimensional structures of different drug targets which includes spike (S) protein, RNA-dependent RNA polymerase (RdRp), 3CLpro (main protease) and papain-like protease. While these structures are the basis for drug discovery research, studies performed in other related viruses, including SARS-CoV and MERS-CoV, have been crucial in formulating therapeutic strategies against SARS-CoV-2. The 3CLpro cleaves the Polyprotein synthesized from the viral +sense single-stranded RNA genome, and is thus one of the most important drug targets.

While the world awaits an effective drug, *de novo* drug discovery would be a highly time consuming and costly venture. Thus, scientists are proposing for repurposing existing drugs for clinical studies, and molecular modeling turns out to be the most potent tool for this. As such, Remdesivir (RdRp inhibitor) and hydroxychloroquine have been suggested and clinical studies have been initiated. Zhang et al. [1] have suggested  $\alpha$ -ketoamides for effective inhibition of the main protease, while Wu et al. [2] have identified a large number of compounds which may potentially inhibit the 3CLpro, using molecular docking.

We have used a similar molecular docking approach using main

protease as the drug target, and screened known protease inhibitors, ketoamides, drugs suggested through repurposing and phytochemicals. The results demonstrated that Ritonavir, a protease inhibitor originally designed against HIV, has the highest potential in inhibiting main protease (article under review). Ritonavir was also reported effective against SARS and MERS [3]. Since the main protease of SARS-CoV-2 shares 96% sequence similarity with SARS-CoV, therapeutics effective against the latter are surmised to be effective against the former as well. Based on this, we recommend that large scale clinical trials with Ritonavir, in combination with other antivirals (including Lopinavir, Remdesivir, Ribavirin, Hydroxychloroquine, etc.) and adjuvants (like Ascorbic acid, Zn<sup>2+</sup>, Melatonin, etc.) be initiated.

## Conflict of interest

None declared.

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