The Therapeutic Development for COVID-19

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Editorial Note

The importance of environmental chemistry has been increasing in the era of industrial advancement. It is also one of the critical issues to consider the chemical compounds and nano-particle chemistry in the environment. The current coronavirus disease 2019 (COVID-19) situation in all over the world has facilitated the development of anti-viral drugs [1]. The emergence of the drug-resistance in the environment would be one of the main concerns in the future. In addition to the drug development, the vaccines have been rapidly developed, which includes the adenoviral-vector based severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spikes (S) protein expressing vaccine [2]. It seems that the proline stabilization, as well asthe S1-S2 cleavage protection in the S protein is critical for the immune response in rhesus macaques [2,3]. The antibody recognizing a whole viral S protein might be needed for the prevention of the SARS-CoV-2 infection. Furthermore, the human angiotensin-converting enzyme 2 (ACE2)-expressed transgenic mice has showed the viral replication of SARS-CoV-2 [4]. The chemical compounds which inhibit the binding of the SARS-CoV-2 particles to the host cells, or the protease inhibitors would prevent the COVID-19. The SARS-CoV-2 might acquire the resistance capacity towards the therapeutics, which raises us the importance of SARS-CoV-2 sequence monitoring and analysis.

The RNA polymerase inhibitors are also targeted in COVID-19 therapeutics. In theory, the viral RNA polymerase recognizes the inhibitors, instead of the viral RNA, as their substrates, which should eventually inhibit the SARS-CoV-2 replication. These RNA polymerase inhibitors, usually as chemical compounds, have the rationale in the therapeutic mechanism. The main concerns include the adverse effects to inhibit human RNA polymerase. The 3D structure of the RNA-dependent RNA polymerase (RdRp) of SARS-CoV-2 bound with small molecule inhibitors at the predicted GTP binding site have been predictively modeled [5]. These small molecule inhibitors of RdRp include FIH, remdesivir (triphosphate), CCT, JPC, SNH, sofosbuvir (triphosphate), and SCHEMBL2157883 [5]. The similarity and difference of SARS-CoV-2 and other RNA viruses should be carefully taken into consideration to target the viral RNA genome replication mechanism [6]. CoVs possess positive-sense, and single-stranded RNA as their genome [6]. The single-stranded RNA viruses in Caliciviridae, Flaviviridae, and Picornaviridae had the 3D structures of RdRp and nucleoside triphosphate (NTP) complexes at a resolution of 2.5 Å as of 2018 [7]. The recognition of RNA by RdRp would be one of the therapeutic targets for RNA genome replication. The inhibition of RNA viral replication mechanism by chemicals seems to be promising as far as the adverse effects and the drug-resistance do not emerge. The SARS-CoV-2 would be rapidly mutating as it is RNA virus, and the binding capacity of their RdRp and small molecule inhibitors may be changing, which suggest the importance of the molecular structure prediction in the therapeutic development of COVID-19. The future advancement in the research to reveal the molecular structure and RNA viral genome mutation, as well as the binding site of the inhibitors in RdRp, may be needed.

References


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