Opinion

Necessity for designing multienzymes-targeting drugs to fight Coronavirus

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Coronaviruses (CoVs) are pathogens that can infect the respiratory, gastrointestinal, liver and central nervous systems of animals. Since the emergence of Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), the possibility of transmission of CoVs from person to person has been proven.[1–3] Emergencies and intermittent outbreaks of new types of CoVs will pose a rising global health threat. On 31 December 2019, World Health Organization was alerted to several cases of pneumonia in Wuhan City, Hubei Province of China. Patients with 2019-nCoV infection, are presenting with a wide range of symptoms leading to severe disease, including pneumonia, respiratory failure and in some cases death.[3] As of January 28, the death toll stood at 131 with *more than 5,000* cases.[4] There is currently no specific antiviral therapy for treating CoV-infected patients and the main treatments are supportive.[1] The genome of CoVs is a single-stranded RNA (size from 27 to 32 kb) with a 5'-cap structure and a 3'-poly-A tail. CoV genomes contain open reading frames (ORFs) encoding structural proteins (peak (S), membrane (M), envelope (E) and nucleocapsid (N) proteins) and non-structural proteins (endoribonuclease, RNA dependent and RNA polymerase, helicase, hexanuclease, papain-like protease (PLP^{pro}), 3C-like protease, also known as the main protease ($3CL^{pro}$), etc.) as well as some accessory proteins.[1,2] Of all proteins, the S, N and E structural proteins have a great interest in the development of vaccines against CoVs (Figure 1).[5]

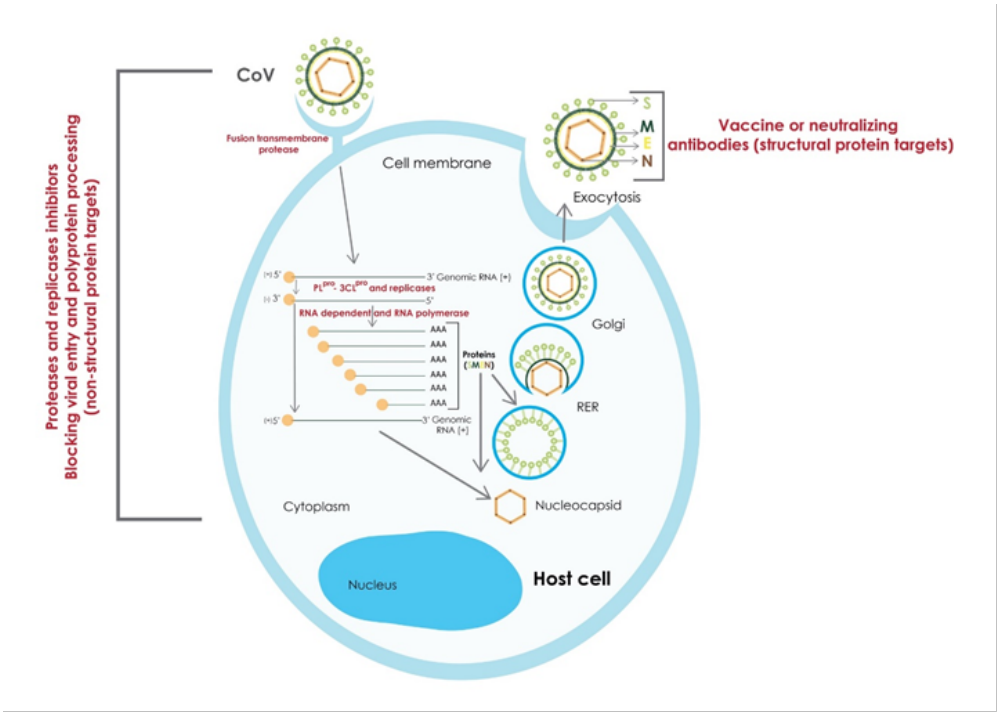

Figure 1 Replication steps that could be targeted simultaneously for development of efficient anti-CoV drugs and vaccines.

The first ideas to target CoV aimed to inhibit viral enzymes, which are exclusively expressed by CoVs and not present in the human genome. Enzyme inhibitors such as CoV RNA-Dependent RNA Polymerase inhibitors and PLP and main protease inhibitors, in combination with other drugs, may be promising candidates for new CoVs treatments. [6–13] Indeed, many studies and patents have been reported in the literature to investigate the properties of nuclease/protease inhibitors and other small molecular inhibitors of the intracellular life cycle of CoVs. [7–13] Some anti-CoV agents have been developed against polymerases, MTases and CoV entry proteins, after the SARS and MERS epidemics. However, none of these anti-CoV agents have not been tested today in clinical trials.[1] The use of

antiviral combination therapy has proven to be effective against the progression to AIDS in HIV-infected patients. Currently, six major classes of antiretroviral drugs are used for the treatment of HIV-infected patients : the RT inhibitors, nucleoside inhibitors and nonnucleoside inhibitors, the protease inhibitors, the integrase inhibitor raltegravir, the fusion inhibitor enfuvirtide (T-20), and the chemokine receptor 5 antagonist maraviroc.[14,15] In line with this, the use of anti-CoV combination therapy based on multienzyme targeted drugs blocking the CoV replication could provide a promising foundation for the development of efficient anticoronaviral therapeutics (Figure 1). The activities of these anticoronaviral drugs could include both the prevention of fusion of the CoV envelope with the receptors on the host cell plasma membrane and the inhibition of viral polymerases and proteases involved in CoV replication.

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Conflicts of interest

Author declares that there is no conflicts of interest.

References

1. Chen Y, Liu Q, Guo D. Emerging coronaviruses: genome structure, replication, and pathogenesis. *J Med Virol*. 2020.
2. Chan JF, Kok KH, Zhu Z, et al. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerg Microbes Infect*. 2020;9(1):221–236.
3. Hui DS, I Azhar E, Madani TA, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - The latest 2019 novel coronavirus outbreak in Wuhan, China. *Int J Infect Dis*. 2020;91:264–266.
4. White J, Newey S, Gulland A. Coronavirus infection: everything you need to know about the outbreak from China. 2020.
5. Yong CY, Ong HK, Yeap SK,et al. Recent Advances in the Vaccine Development Against Middle East Respiratory Syndrome-Coronavirus. *Front Microbiol*. 2019.
6. Ouertani A, Neifar M, Ouertani R, et al. Effectiveness of enzyme inhibitors in biomedicine and pharmacotherapy. *Adv Tissue Eng Regen Med Open Access*. 2019;5(2):85–90.
7. Tong TR. Therapies for coronaviruses. Part 2: inhibitors of intracellular life cycle. *Expert Opin Therap Pat*. 2009;19(4) :415–431.
8. Olsen DB, Tomassini JE, Mao SS, et al. Inhibiting coronaviridae viral replication and treating coronaviridae viral nfection with nucleoside compounds. Patent US20040259934. 2004.
9. Shen J, Jiang H, Shen X, et al. 3D-structure model of SARS coronavirus 3CL protease and anti-SARS drugs. Patent US20060142383. 2006.
10. Fujii N, Yamamoto N, Anti-coronavirus drug patent 20060223847. Tokyo (JP). Arigen, Inc; 2006.
11. Chan JF, Chan KH, Kao RY, et al. Broad-spectrum antivirals for the emerging Middle East respiratory syndrome coronavirus. *J Infect*. 2013;67(6):606–616.
12. Cheng KW, Cheng SC, Chen WY, et al. Thiopurine analogs and mycophenolic acid synergistically inhibit the papain-like protease of Middle East respiratory syndrome coronavirus. *Antiviral Res*. 2015;(115):9–16.
13. Wang Y, Sun Y, Wu A, et al. Coronavirus nsp10/nsp16 Methyltransferase Can Be Targeted by nsp10-Derived Peptide In Vitro and In Vivo To Reduce Replication and Pathogenesis. *J Virol*. 2015;89(16):8416–8427.
14. Wang Y, Lv Z, Chu Y. HIV protease inhibitors: a review of molecular selectivity and toxicity. *HIV/AIDS Res Palliat Care*. 2015;(7):95–104:
15. Sierra S, Walter H. Targets for Inhibition of HIV Replication: Entry, Enzyme Action, Release and Maturation. *Intervirolgy*. 2012;55(2):84–97.