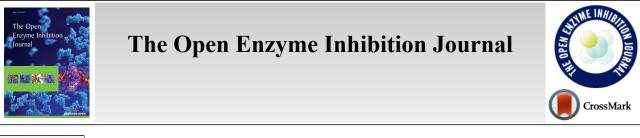
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## EFWQTICN

## Coronavirus and Enzymes: What the Past Told us?

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Novelty always frightens, provoking overreactions. On the other hand, the strategy of viral infection, including that of coronavirus (COVID-19), originates from ancient times and can be summarized, as 1) entry into host cells, 2) interfering with host genetic program to duplicate virus entity; 3) infection into surrounding cells. These are the strengths of the viruses but also their weaknesses since it identifies possible targets to prevent infection. At each step of viral infection, viral enzymatic reactions are observed, which may be similar to those occurring in another closely related family of viruses. COVID-19 is related with 88% to two bat-derived severe acute respiratory syndromes (SARS)-like coronaviruses (bat-SL-CoVZC45 and bat-SL-CoVZXC21, collected in 2018 in Zhoushan, eastern China), SARS-CoV (about 79%) and MERS-CoV (about 50%) [1]. The penetration of the COVID-19, similar to that of SARS-CoV, into the infected cells is triggered by the interaction of a protein on the surface of the virus with a receptor angiotensin-converting enzyme 2 (ACE2) on the infected cells [2]. Preventing interaction between the viral protein on its surface and the cell receptor, using a soluble version of the viral receptor, angiotensinconverting enzyme 2 fused to an immunoglobulin Fc domain, is a proposed plan to prevent coronavirus infection [3]. This modified ACE2 will selectively interact with the viral protein and not with the cell, protecting physiological function of ACE2 [3]. Several viral enzymes are possible targets to design drugs for stopping viral infections. Once the virus penetrates into the host cell, it interferes with the genetic program. Possible target is the viral RNA-dependent RNA polymerases to avoid viral duplication. Remdesivir, a nucleotide analog, can inhibit the viral RNA-dependent RNA polymerase and had broad spectrum of antiviral activities against several RNA viruses including SARS-CoV and MERS- CoV [4], stimulating hope that Remdesivir treatment could be also effective to treat

\* Address correspondence to this author at the ICBMS UMR5346, Université Lyon 1, 43 Bd 11 Novembre 1918, Villeurbanne, France; Tel: 33 4 27 46 57 21; E-mail: rbuchet@univ-lyon1.fr patients with COVID-19. Additional viral enzymes such as integrases and proteases, which are active during other steps of viral life cycle, can be targeted for developing drugs to disrupt viral life cycle. For example, the viral protease stimulates an active infectious virion after budding from the infected cell. The protease inhibition causes improper viral protein maturation, decreasing viral infection. Based on the successful curative properties of ritonavir (an aspartyl protease inhibitor of HIV) against HIV, combination therapy with ritonavir and lopinavir was initiated to a 47-year-old man with COVID-19, leading to quick improvement of clinical symptoms [5]. To conclude, viral enzymes are adequate targets to treat viral diseases due to their specific actions during different steps of viral infection. This is one possible way for the development of alternate drug therapies other than vaccines. Efficient treatments based on inhibitors of viral enzymes against past viruses could be effective against new closely related viruses.

## REFERENCES

- Lu R, Zhao X, Li J, *et al.* Genomic characterisation and epidemiology of 2019 novel coronavirus: Implications for virus origins and receptor binding. Lancet 2020; 395(10224): 565-74.
  [http://dx.doi.org/10.1016/S0140-6736(20)30251-8]
  [PMID: 32007145]
- [2] Li R, Qiao S, Zhang G. Analysis of angiotensin-converting enzyme 2 (ACE2) from different species sheds some light on cross-species receptor usage of a novel coronavirus 2019-nCoV. J Infect 2020; 80(4): 469-96.
- [3] Kruse RL. Therapeutic strategies in an outbreak scenario to treat the novel coronavirus originating in Wuhan, China [version 1; peer review: awaiting peer review] F1000Researe 2020; 9:72.
- [4] Gordon CJ, Tchesnokov EP, Feng JY, Porter DP, Gotte M. The antiviral compound remdesivir potently inhibits RNA-dependent RNA polymerase from Middle East respiratory syndrome coronavirus. J Biol Chem 2020; pii: jbc.AC120.013056. [http://dx.doi.org/10.1074/jbc.AC120.013056]
- [5] Han W, Quan B, Guo Y, *et al.* The course of clinical diagnosis and treatment of a case infected with coronavirus disease 2019. J Med Virol 2020; 92(5): 461-3.
  [http://dx.doi.org/10.1002/jmv.25711] [PMID: 32073161]

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