Immediate Repurposing of the FDA Approved Drug (TRL6) to Treat or Prevent Coronavirus by Inhibiting the Human Protease Furin

Dr. Richard Watt – Brigham Young University – CSO REVITALE Pharma

Inhibiting the Viral Lifecycle

Viruses can jump from animals to humans when the virus mutates by taking advantage of human receptors that allow internalization of the virus into cells. The new coronavirus SARS-CoV-2 (COVID-19) has mutation in the spike glycoprotein that introduced a new Furin cleavage site (http://www.virology.ws/2020/02/13/furin-cleavage-site-in-the-sars-cov-2-coronavirus-glycoprotein/). Human Furin in the respiratory tract plays a role in cutting proteins to make them active. A virus takes advantage of Furin and other human proteases to cut the viral proteins into a form recognized by human cells, so the virus is internalized. This new mutation allows SARS-CoV-2 to infect humans. Similar cleavage sites are present in different forms of the flu (swine, bird etc.) and present in Ebola and Marburg virus. Drugs targeting Furin have great promise for treating COVID-19. See https://www.theatlantic.com/science/archive/2020/03/biography-new-coronavirus/608338/.

Breakthrough. Currently no Furin inhibitors are approved for medical use (Couture et al. therapeutic uses of furin and its inhibitors: a patent review, https://doi.org/10.1517/13543776.2014.1000303). The Watt Lab at Brigham Young University recently discovered that FDA approved drugs that can be repurposed as Furin inhibitors. This discovery opens opportunities for treating many diseases including viral outbreaks. We have already communicated with the FDA for phase 2 clinical trials and received a response that our goal is reasonable.

Our calculations show these drugs bind tightly to the catalytic site of Furin. Additionally, we have strong data that these drugs inhibit furin in purified enzyme assays, in tissue culture and in animal studies.

In a 2004 SARS outbreak Nelfinavir was shown to lower viral load (Yamamoto, et al. Biochem Biophys Res Commun. 2004 Jun 4;318(3):719-25). Ritonavir, Lopinavir, Indinavir and Saquinavir were tested but were less effective. A recent computer docking study on the new 2019-nCoV virus (https://www.biorxiv.org/content/10.1101/2020.01.27.921627v1) showed Nelfinavir also binds to the coronavirus protease and inhibits viral protein processing. Therefore, Nelfinavir can inhibit multiple steps in the 2019-nCoV lifecycle.

A recent Lancet article gives the clinical features of 2019-nCoV (Volume 395, Issue 10223, 15–21 February 2020, Pages 497-506), and discusses that Ritonavir/Lopinavir have shown benefit in other SARS and MERS outbreaks. Our computer modeling shows that these drugs can also inhibit furin but with less potency than Nelfinavir.


The Watt lab has demonstrated that Furin inhibition with Nelfinavir blocks the activation of Hepcidin and MMPs making Nelfinavir a potential treatment for sepsis. Combined, Nelfinavir’s ability to inhibit steps in the coronavirus lifecycle and inhibit pathways associated with sepsis make the drug a viable candidate for an immediate human clinical trial following the 505(b)(2) drug repurposing pathway to treat and prevent coronavirus.