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Letter to the Editor

Will Entry Inhibitors Offer New Hope for COVID-19 Patients?

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COVID-19, a type of coronavirus first identified in Wuhan, China, has recently become a pandemic! While not a virologist, I have identified several novel treatments to different malignancies and have been requested to publish my thoughts on COVID-19. Following are my ideas to assist the Coronavirus Task Force.

First, communicating through the journals with medical professionals is crucial. The first challenge I encountered when studying coronaviruses is a language barrier! Some of the literature is not translated from Chinese. Surely our experts can assemble a translation team to translate articles originating in China, so that English-speakers can be better informed on any information gleaned about COVID-19 in China.

When approaching the identification of a cure or treatment to any disease, we must first ask ourselves to identify the unknown. Thus, we must ask "What is it that I do not know?".

This, in Eastern Indian culture, is referred to as "identifying the lacuna," or dark cave. For example, as a biochemist, I have not been trained in the difference between SARS and COVID-19. Is COVID-19 the same viral disease as SARS-CoV2? Some sources indicate that this is the case [1].

This should be verified. Any clarification regarding similarities to what is known on SARS should be considered. Also, any differences that could be exploited should be documented and shared with the medical community.

How should we approach defining the unknown? First, I would consider viruses with successful treatments and analyze their methodology for any similarities to COVID-19.

For example, is there any aspect in the design of HIV drugs that could cross over? We know that the virions must attach themselves to the host cells. Could a method be designed to coat the virions or coat cells such that attachment is sterically hindered? What proteins are required for COVID-19 to infect or replicate? These proteins are known for HIV and include: Gp120 interaction with helper T-Cells CD4 receptor and with the transmembrane protein, CXCR4 [2]. A similar transmembrane protein in macrophages is CCR5 [3]. HIV's gp41 is known for inserting itself into the host cells' membranes, pulling viral and cellular membranes together [4]. We must identify similar protein interactions between our host cells and COVID-19 proteins. For example, coronavirus S proteins bind cells metalloprotease amino peptidase N [5]. Once such interactions are identified, drugs that prevent these crucial interactions can be designed such as how entry inhibitors were designed to block gp41 in HIV. Enfuvirtide is a fusion inhibitor [6] HIV drug that should be investigated to determine if it will successfully prevent infection by COVID-19.

A coronavirus viral RNA polymerase is required to translate the proteins that COVID-19 requires [5]. Can repressors be designed to sit on the viral RNA that is translated into the replicatory proteins employed by COVID-19? Can we design an inhibitor for this viral RNA polymerase? Asking these basic questions should assist the design of drugs and vaccines to intervene in the capture of victims by COVID-19.

What suggestions can aid us now while we wait for novel drugs to be developed? While not typically a proponent of repurposing drugs, this critical time with an accelerating pandemic, calls for drugs that can be brought to market quickly! Test laboratories should investigate if any drugs for other known viruses are effective against COVID-19. If fortunate, these drugs could be approved for use more quickly than novel drugs.

Finally, which over-the-counter and presently approved prescription drugs can be employed? For example, do broad spectrum antivirals exhibit any efficacy in COVID-19 patients? Also, guaifenesin increases fluid production in the lungs [7] so that pathogens such as virions are expelled versus becoming attached to the bronchial epithelial cells. This strategy employs the phlegm of our innate immune system defenses [8] and can be purchased under the brand name Mucinex at any local drug store! Could early administration of guaifenesin interfere with COVID-19 virion attachment to host cells in the lungs of exposed patients?

Further, organ damage caused by COVID-19 analyzed post-mortem may provide additional understanding on how this virus attacks, survives (such as nutrients it requires) and replicates. Knowing and reporting the answers to these and the aforementioned questions should shed light on our perception of COVID-19 and its method of infecting patients. We can win in the war on this pandemic by gaining understanding. Such insight will permit survival, just as it has permitted mankind to overcome our predators since the caveman.

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