From: Fauci, Anthony (NIH/NIAID) [E]

Sent: Fri, 24 Apr 2020 00:35:33 +0000

To: Lerner, Andrea (NIH/NIAID) [E]

Subject: FW: Another Possible Tool in The Fight Against SARS-CoV-2?

Pleas take a look and figure out where to send it.

From: Gary Radin < GRadin@dhs.lacounty.gov>

Sent: Thursday, April 23, 2020 8:31 PM

To: Fauci, Anthony (NIH/NIAID) [E] (b) (6) >

Subject: Another Possible Tool in The Fight Against SARS-CoV-2?

Dr. Fauci---Forgive the crude and unsolicited manner in which I am attempting to reach out to you but I don't really KNOW any other way!

I am not a medical doctor nor am I a principle investigator. I am just a Cytologist employed in the Anatomic Pathology department at LA County-USC Medical Center here in Southern California.

But I have been reading a lot--- and in my own exploration I have come across several articles which suggest the possibility of using a class of agents called

SPHINGOSINE-1-PHOSPHATE RECEPTOR AGONISTS in combination with antivirals like oseltamivir (or perhaps Remdesivir?) to treat both the viral pathogen responsible for the current pandemic as well as the runaway immune response of the host leading to the oft fatal cytokine storms.

Apparently these compounds have been approved for flare-ups of multiple sclerosis, and have even been tried on Alzheimer's patients. The commonly known drug is FINGOLIMOD. But these papers that I have cited for you below seem to indicate that structural analogs of this compound could be important in damping down the dysregulated pro-inflammatory cascades which seem to be leading to DIC, alveolar exudates and diffuse alveolar damage, capillary leak syndrome and ultimately the multiple organ failure that is killing an unacceptably high number of people.

The fly in the ointment Dr. Fauci here is that these S-1-PR agonists have only been demonstrated to be effective in non-human primates and other mammals. And much of these studies on these compounds has been done not on coronaviruses but on influenza viruses. So it would be a gamble. But is that not how we have learned much about human health and disease is by the gracious sacrifice of our animal cousins? And might it not be a general effect that these sphingosine derivatives have on viral sepsis so that maybe what works for influenza might work for the coronavirus?

In the dire situation that many of the most critically ill COVID 19 patients find themselves, it seems they are on the precipice of a rapid demise once they begin to show certain key laboratory results---(spikes in D-DIMER, C-Reactive Protein, Serum Ferritin, prolongation of