COVID-19, our new normal?

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The current threat that COVID-19 presses on us will go down in history as one of the most eye opening events that peers in my generation will have faced. The virulence displayed by this virus has had deadly consequences all over the world, and been spreading exponentially fast. With most countries be unprepared for this new virus, it has been tough to contain. This virus has a unique composition, and it infects at very specific sites in the body. While currently more testing and trials need to be accomplished before a vaccine or treatment is developed for COVID-19, there have been some sites identified for potential action.

COVID-19 belongs to the virus family of *Coronaivrinae*, or Coronavirus. Coronaviruses are unique as they are a type of positive strand RNA virus that bind to the ACE2 (Angiotensin-converting enzyme 2) site in our lungs (1). COVID-19 being a RNA virus can be both good and bad depending on certain perspectives. Being a RNA virus, it will mutate at an exponentially higher rate than a DNA virus could. Simply put, DNA viruses have the self correcting mechanisms to fix errors in genetic replication and prevent over mutating, while RNA viruses don't have them and become genetically unstable with not being able to correct errors in genetic replication. They have high rates of replication that leads to a high rate of mutation, where almost 1-2 mutations in offspring can occur(6) per cycle. This can be bad, as it makes it tough for scientists to find and develop medicine or treatment to attack certain sites on COVID-19, because those sites are constantly evolving and changing. For purposes relating purely to the survival of the RNA viruses these mutations can be helpful to maintain viability and survivability. However, most of these mutations are not helpful to increase viability and survivability and can leave each generation of RNA viruses to leave fewer and fewer offspring

each time. This makes it a good thing, as there could be slight hope for COVID-19 to over evolve to the point of self-extinction. While in theory this could happen, no health organization should be banking on it to eventually happen as other RNA viruses in human history have become staples of our lives now, and have shown no signs of leaving (like MERS). For different reasons, MERS has stayed active due to being transmitted through camels and the roles they play in middle eastern lifestyle (7).

The binding site of COVID-19 in most hosts is ACE2. ACE2 acts as an important regulator for the renal system by maintaining homeostasis of blood pressure and other renal-angiotensin systems (3). ACE2 had been discovered as the key site of attachment for COVID-19, which in and of itself brings some big consequences in the renal system. The primary function of ACE2 is to convert angiotensin 2 to angiotensin 1-7. Higher levels of angiotensin 2 in the system have been correlated to higher levels of hypertension from mice studies (4). Due to ACE2 only having one primary active site, if it is being inhibited by COVID-19 binding to it there can be issues on regulating the amount of angiotensin 2 as well, which may lead to a spike in blood pressure as angiotensin 2 cannot convert to angiotensin 1-7. The body responds to hypoxia (the inability of oxygen to reach vital tissue and organs) by having an uptick in levels of angiotensin 2 in all cells of the system (3). This uptick induces pulmonary vasoconstriction which is key in letting oxygen be available to travel to the key organs and tissues(4). While this is very medically related, ACE2's role in biochemical regulation is important and if impeded by COVID-19, can have dire consequences on the host in terms of respiratory issues and organ failure due to vasoconstriciton.

As for treatments for COVID-19, while nothing is firmly released on the market for treatment yet, many potential forms of treatment are being tested for release to the general

public. While there wouldn't be one cure all drug for COVID-19, creative forms of treatment are being investigated to inhibit the main protease of COVID-19. The potential inhibition of this protease (Mpro) can lead to blocking of the polyproteins of COVID-19, which are key to further replication. Polyproteins are important proteins that produce hormonal polypeptides through use of cleavage, and viral proteases are specific enzymes that cleave specific peptide bonds. Blocking this, prevents important protein precursors from being cleaved and then be used for more viral replication(8). Block replication of this deadly virus could mean less spread. One proposed path is using alpha-ketoamide inhibitors (5) as the base for developing inhibitors against the virus. These inhibitors are able to specifically target and inhibit the main viral proteases, as they are completely different to other proteases in our own cells. By analyzing different crystal structures of alpha-ketoamide's there's hope to find one that can interrupt the protease activity in the virus, and work to destroy it entirely. To see if the alpha-ketoamide's could work as potential inhibitor of COVID-19, the lab reference would make several modifications to their base drug and use crystal structures to dock their drug on the main protease (Mpro) and see what affects these drugs would have against COVID-19.

Another creative, but potentially difficult path of treatment is to use organosulfur compounds found in garlic oil against COVID-19 (2). These organosulfur compounds had two effects against the virus, with the first being temporarily inhibiting the ACE2 protein. Due to the strong amino acid interactions between the organosulfur compounds and ACE2, the virus cannot dock and enter the host cell. Another way the organosulfur compounds effect the virus, is by interrupting the hydrogen bonding and, cation bonding, and ionic interactions within the virus itself and making it nonviable. While there hasn't been in vivo testing over this, and it's only been evaluated in the docking simulations mentioned earlier, it does offer a different natural

alternative after potential further development (though it still may be a longshot, and only work in nonrealistic perfect conditions). Potentially, only extremely concentrated levels of these organosulfur compounds would have drastic affect on the virus, so much so that the average garlic consumer would not see much or any affect.

This is truly a virus that has put the whole world at risk. Almost every age group is susceptible, and it spreads so rapidly that it has reached most corners of the Earth. More testing needs to be done on finding ways to treat it, but more importantly people need to obey social distancing guidelines to help the most vulnerable of our population over this threat. It is something that realistically may not just disappear, and something that brings a new normal to our lives.

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