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Exploring ACE/ACE2

The ongoing development and spread of covid19 have proven to become an experience that brings forth many different thoughts and feelings. With the foremost feelings being confusion and fear. Those feelings have taken a toll on not only everyday people and activities but also on the scientific community and health care infrastructures. With no vaccine in sight, the mystery of covid19 has proven to be overwhelming for the science community, which has led to observing all possibilities of not only destroying the virus but potentially inhibiting it from entering into the human body in the first place. This is where studying ACE and ACE2 become relevant and interesting in an attempt to observe its effects on a human reaction model when knocked out.

ACE stands for angiotensin-converting enzyme. ACE is an enzyme that is most prevalent on the surface of capillary endothelial cells. ACE's job is to convert angiotensin 1 to angiotensin 2 by removing several amino acids. ACE2, on the other hand, is an opposing molecule who's job is to convert angiotensin 2 back to angiotensin 1. Angiotensin 2 has been proven to have a negative effect on the body, such as raising blood pressure, and it is the cause for a large number of cardiac issues in addition to hypertension. Having ACE2 present to reverse the negative angiotensin 2 back to angiotensin 1 has proven to be beneficial and can sometimes fill in as an augmented alternative to the traditional ACE inhibiting drugs that are currently prescribed. Despite ACE2 being beneficial in many crucial applications, it has been proven that ACE2 also is a receptor for covid19 spike glycoprotein structure leading to the incorpo-

ration of covid19 into the body relatively easily with ACE2 acting as a transport vector. With that being known, a lot of researchers are being pushed in the direction of understanding the makeup of ACE2 and preventing covid19 from entering the body even if that means inhibiting ACE2. With the possibility of inhibiting ACE 2 in mind, I decided to search for the ACE and ACE2 genes in the Recon3D human model and identify the reactions associated with the two genes and knock them out to observe the effect (if any) on the model and the growth rate of a cell.

Fortunately, both genes were present in the Recond3D model, which made it easy to identify the reactions associated with the 2 genes. ACE was shown to only be present in one reaction RE2445E. ACE2 was found to be present in the same reaction as ACE; however, ACE2 was also shown to be present in 20 other reactions. In order to observe all possibilities, I decided to knockout both genes ACE and ACE2 in addition to all 20 reactions related. The knockout was done using the provided FBA analysis python script slightly edited to knockout out the genes/ reactions of interest and return the results in an easily understandable output. The results, unfortunately, proved to be fruitless, with the growth rate remaining the same throughout the model of each knockout of the genes and associated reactions. These results were disappointing but not terribly surprising due to the understanding of how complex the Recond3D model is.

Even though the results I observed of the knockout didn't give any impressive results, I still find it essential to explore this possible solution of disrupting covid19 binding to ACE2. I believe knocking out the genes, and associated reactions is a good

starting point, and for future experiments, I would consider knocking out the preluding reactions of those genes.