Evaluating the Efficacy of Repurposed and Modified Traditional Eastern Medicinal Compounds on Coronavirus Family Specific Target Structures

Lee, Brian (School: Plainview-Old Bethpage John F. Kennedy High School)

It has been approximately 17 years since the severe acute respiratory syndrome coronavirus (SARS-CoV) epidemic and the world is presently facing the COVID-19 pandemic caused by SARS-CoV-2 virus. Both are positive sense retroviruses and currently, researchers are exploring small molecule based interventions to the different specific proteins produced by this virus. One such protein, integral to the survival of SARS-CoV-2, is 3CLpro which works as a protease to cleave the two distinct polyproteins assembled from the single RNA strand that is injected by the virus. Previous 3CLpro analyses showed that this protease was important to its metabolic processes as well, making it a viable target. Altering the active site of this protease or its important residues could change its configuration, restricting any sort of cleaving, resulting in useless polyproteins and rendering the virus mute. Additionally, SARS-CoV-2 uses an RNA pseudoknot to induce programmed RNA -1 ribosomal frameshifting in order to create two separate polyproteins. Altering the binding site between the pseudoknot structure and ribosome could result in a faulty polyprotein or the creation of only one polyprotein, deleting several important proteins required by the virus. This project identified the active sites of both molecules, the optimal residues that are integral to the structure, and current ligands/drugs that are being manufactured and/or tested to restrict them. Using docking systems such as AutoDock Vina, it was determined which ligands had the best compatibility with the molecule and using molecule design tools, added to their structures to better fit the target molecules.

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