The Effect of Amino Acid Mutagenesis on the Binding Affinity of SARS-CoV-2 Monoclonal Antibodies

Joshi, Kartik (School: Little Rock Central High School)

The purpose of this project was to see if the mutation of an amino acid in a SARS-CoV-2 monoclonal antibody can increase the antibodies' binding affinity. My hypothesis is that I will be able to improve the affinity of the monoclonal antibodies by amino acid mutation in the hypervariable region, specifically in the heavy chain hypervariable region 1 (Threonine (THR) 28, mutated to Aspartic Acid (ASP)). To begin, I needed to decide which PDB I needed to use. Then, I ran the FASTA sequences for 20 PDBs in Clustal Omega 2, allowing me to see similarities and differences between the various monoclonal antibodies. I decided to choose PDB ascension number 6xc3, as its constant region was well conserved. I chose to run the 28th amino acid as it was constant among many of the monoclonal antibodies. I ran these PDBs in PyMOL to measure the interactions between the antibody and the Receptor Binding Domain (RBD). Running the PDB in PyMOL, I then used the mutagenesis tool to mutate the threonine into aspartic acid. After mutating the amino acid on the heavy chain, the interactions between the antibody and the RBD increased. Prior to mutagenesis, the Threonine had two interactions with the RBD. However, after mutating the 28th amino acid into aspartic acid, the number of interactions increased from 2 to 5. In conclusion, my hypothesis was shown to be correct. Due to the increased number of interactions, the chain of the antibody is holding on to the RBD of the SARS-CoV-2 virus much stronger than it was before, likely reducing the probability that the virus can escape the antibody. This has an important application, as it indicates that monoclonal antibodies can be mutated to be more reliable in treating COVID-19.