Computational Design, Docking, and Analysis of Novel Aryl Sulfone Compounds as Potential NNRTIs

Adwankar, Rohan (School: Irvington High School)
Morgaonkar, Aarya (School: Irvington High School)
Zhang, Andy (School: Irvington High School)

HIV affects millions of people globally. Due to the high mutation rate of HIV, it is important that novel drugs are constantly found to combat new strains. NNRTIs are allosteric inhibitors that bind to the HIV reverse transcriptase and prevent replication. IAS derivatives have been found to be highly effective against mutant strains of HIV-1 reverse transcriptase. We designed molecules using aryl sulfone scaffolds paired with cyclic compounds as potential NNRTIs through the design and docking of 160 novel NNRTI candidates. We explored which combination of cyclic compounds and aryl sulfones would result in the best NNRTI candidates and hypothesized that an indolyl aryl sulfone scaffold and pyrimidine would produce the compounds with the best binding affinity. Our hypothesis was refuted as a combination of styrene and IAS had the best average binding affinity. This research found 52 molecules designed in this procedure with higher or equal binding affinities to the successful IAS derivative when docked to HIV-1 reverse transcriptase. We also docked our molecules to mutant HIV reverse transcriptase enzyme to see its efficacy at docking to mutants compared to IAS derivatives explored by previous researchers. These docking scores were used to train a machine-learning algorithm capable of identifying molecules that have a higher binding affinity than the aforementioned IAS derivative. This model serves as a proof of concept that it is possible to develop a cheminformatics machine learning algorithm able to predict whether molecules would have high or low binding affinities, furthering the development of cheminformatics algorithms in the future. These findings contribute to the search for novel NNRTIs and expand knowledge of the characteristics of the NNRTI pharmacophore.

Awards Won:
Second Award of $2,000