

Synthesis of Group-1 Neuraminidase Enzyme Inhibitors

When Tamiflu was originally developed, the drug was designed based on the structure of the group-2 neuraminidase enzyme. When bird flu(H5N1) hit the United States in 2008, scientists were able to crystallize the group-1 neuraminidase enzyme and discovered the active site pocket was much larger compared to the previously determined group-2 active site. My research aims to synthesize a library of compounds that should bind the active site of group-1 neuraminidase. The library of compounds chosen should map the electronic and spatial requirements of the active site, guiding future inhibitor development. Our synthetic targets were made by means of coupling an organic molecule to a library of selected amino acids. Next steps included purification of crude products via column chromatography, removal of protecting groups, and final purification by HPLC. Structure and purity was confirmed by NMR. Once the library of compounds is complete and we have a working enzyme assay, we will measure their binding affinities.