Designing New Leads for Neuraminidase using *Ab-Initio* Approach

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Influenza constitutes one of the most important upper respiratory tract infections regarding morbidity, and mortality. Influenza A (H1N1) virus is a subtype of influenza A virus and was the most common cause of human influenza (flu) in 2009, this new subtype A/H1N1 is a re-combined virus by human, swine, and avian influenza viruses with a high transmissible ability among human beings. Due to high rate of mutations virus get drug resistance to currently marketed drugs. Influenza A viruses are categorized into antigenic HA and NA subtypes: 16 HA (H1–H16) and 9 NA (N1–N9) antigenic subtypes. This new strain confers resistance to M2 channel inhibitors Amantadine (AMT) and Rimantadine (RMT). Fortunately, the neuraminidase (NA) inhibitors Oseltamivir and Zanamivir are still effective against the new virus. However, as these drugs are widely used, neuraminidase has faced a selection pressure and possible mutants have occurred making the drug target less effective. Sub-type specific NA mutations have been found which are resistance to NA inhibitors, eg. H274Y and N294S has been identified in N1. In addition, several other neuraminidase mutants like E119G/A/V/D, R292K and R152K in the N2 and N9 subtypes have been found which are being found resistance to Zanamivir. Also Oseltamivir is widely used to treat the patients infected with pandemic H1N1(2009) virus, the new influenza strain including H274Y mutation has been separated in clinical recently which can be the mode of study using Molecular Docking and binding energy calculation to study the drug targets in different mutants. Current work is in the direction of designing and finding new lead molecules which can inhibit the virus in wild type and mutants both. Few molecules has been obtained from the approaches used having common structures based on the hybridization state that shows favorable binding with the mutants H274Y and N294S and with wild type i.e. 2HU4.