CONCLUSION

During a docking procedure we were able to trace the binding pathway for Oseltamivir to the binding site of Wild type and H274 mutant H5N1 neuraminidases. The two well-known loops 150 and 430 have been recognized to be important roles in guidance the drug to the binding pocket despite their considerable flexibility. The function of D151 for upturned movement of Oseltamivir during this pathway docking procedure has been unexpectedly revealed. Along the pathway for H274Y, Oseltamivir does not interact with loop 430. Therefore, Oseltamivir does not have stable position and strong connection with residues in order to enter the binding site of H5N1. On the other hand, the bulkier Y274 residue forces the carboxyl groups of the E276 to move farther toward the binding site, this motion made a change in rearrangement of the neighboring residues. However, two hydrogen-bonds in the interaction between E276 and R224 were still in observation similar to the hypothesis of Supot et al. 2009. In terms of drug resistance, residue E276 and loop 430 were the key changes in the crystal structure of the H274Y mutant, obstacles along the way into the binding pocket are may reason of causing drug-resistance.

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