Top-Leads for Swine Influenza A/H1N1 Virus Revealed by Steered Molecular Dynamics Approach

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Abstract: Since March 2009, the rapid spread of infection during the recent A/H1N1 swine flu pandemic has raised concerns of a far more dangerous outcome should this virus become resistant to current drug therapies. Currently oseltamivir (tamiflu) is intensively used for the treatment of influenza, and is reported effective for 2009 A/H1N1 virus. However, as this virus is evolving fast, some drug-resistant strains are emerging. Therefore, it is critical to seek alternative treatments and identify roots of the drug resistance. In this paper we use the steered molecular dynamics approach to estimate the binding affinity of ligands to the glycoprotein neuraminidase. Our idea is based on the fact that the larger is the force needed to unbind a ligand from a receptor the higher its binding affinity. Using all-atom models with Gromos force field 43a1 and explicit water, we have studied the binding ability of 32 ligands to glycoprotein neuraminidase from swine flu virus A/H1N1. It is shown that four ligands 141562, 5069, 46080 and 117079 from the NSC set are the most promising candidates to cope with this virus, while peramivir, oseltamivir and zanamivir are ranked 8, 11 and 20. Our prediction may be useful for the therapeutic application.