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Computer aided protein structure based molecular docking approach to discover new antimalarial drug leads

Malaria is by far the most important tropical parasitic disease, and kills more people than any other communicable disease except tuberculosis. The causative agents in human are four species of *Plasmodium* protozoa: *P. falciparum, P. vivax, P. ovale* and *P. malariae.* Of these, P. *falciparum* accounts for the majority of infections and is the most lethal. *P. falciparum* has developed resistance to drugs including chloroquine and mefloquine. Although some new drugs have appeared in the last 20 years, new especially inexpensive and affordable drugs are badly needed. P. *falciparam* proliferation in human erythrocytes requires purine salvage by hypoxanthine-guanine-xanthine phosphoribosyltranserase (HGXPRTa5e). Thus, interfering with purine salvage could be an effective way of killing these organisms. In this presentation we seek to demonstrate the feasibility of computer aided protein structure based design approach to discover new drug leads to block purine salvage in the parasitic protozoan Plasmodium *falciparam.* The software package DOCK 4.0 was used to screen the Maybridge chemical database for potential HGXPRTase inhibitors. We found that the docked immucillinHP reproduced the crystallographic binding mode. The root mean square deviation (RMSD) of the docked immucillinHP with respect to the X-ray crystal structure was 0.784 A. The total of 22000 compounds have been docked and the 5 compounds with highest negative energy scores along with docked immucillinHP were shown below. The energy soccer is measured in kJ/mol and given in parenthesis. Some of these compounds in the present study may serve as a starting point for further molecular design of novel antimalarial drugs.