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IGER/RCMS Seminar

Theoretical Chemistry Colloquium

April 1, 2015 (Wed), 16:00-17:00

RCMS, 2nd floor, Chemistry Gallery

Molecular dynamics studies on infectious diseases of humans

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Abstract: We aimed at gaining insight into molecular details on the target proteins related to certain human diseases and health problems including influenza and cancer. The functional machinery of such proteins as well as drug inhibition, source of drug resistance and drug screening were studied using various computational techniques, i.e., homology modeling, combinatorial chemistry, molecular dynamics (MD) simulation, combined quantum mechanics/molecular mechanics (QM/MM) and three-dimensional reference interaction site model (3D-RISM). As a result, several questions have been revealed, for example, why and how high pathogenic HA of influenza H5N1 virus was experimentally better cleaved by subtilisin-like serine protease (furin) than the low pathogenic hemagglutinin; how available anti-influenza drugs can well inhibit the neuraminidase and/or M2 protein but less susceptibility against their mutants; and how proton is selectively transported throughout M2 channel. The combinatorial chemistry and steered MD were successfully used to design and screen the potent compounds from available databases for inhibiting influenza neuraminidase and hepatitis C NS3/4A protease, respectively. In addition, the cleavage inhibition of NS3/4A by boceprevir and telaprevir has been explored using the semi-empirical QM/MM MD simulations. As a result, the acylation step is occurred in the concerted manner, with a consequence of inhibitor covalently bonded with enzyme formed in the last step of reaction.

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