Molecular Dynamic Simulations of the HIV Protease Subtype C vs. B

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Abstract

AIDS kills millions of people worldwide. Those victims that acquire AIDS are first infected with the HIV virus before developing AIDS. One of the major targets in anti-HIV therapeutics is protease inhibition. The HIV protease is a major cog in the reproductive process of the AIDS virus. The protease, cleave gag-pol proteins creating new viral particles, which later are bud from the host cell to infect other cells. Therefore, protease inhibition prevents the maturation and then spread of the virus. Most of the current research on the AIDS epidemic has been done only on the virus HIV-1 subtype B. HIV-1 subtype C is a viral strain, which affects far more people in the world in particular those in developing countries. It has been documented that HIV-1 subtype C has a higher viral load in the blood, spreads faster than any of the other subtypes, and mutates at a fast rate. Mutations in the HIV protease brought on by drug treatment make the protease an elusive target. Currently, victims of AIDS are often forced to take drug cocktails to fight the virus at various keypoints in the lifecycle, affecting the victims financially through the cost of the medicines and their quality of life by the shear volume of drugs they are forced to take. A better understanding of the dynamic motion of the HIV protease would allow researchers to potentially develop new compounds to fight the HIV virus. In this work we present molecular dynamic simulations of over 12ns combined using the crystal structures of two FDA approved inhibitors, nelfinavir, and indinavir complexed with HIV-1 subtype C protease. These simulations are the first performed on the HIV-1 subtype C protease (HIV-PRC) with the drugs extracted from the active site. Analysis of results show three distinct conformations of the loop separations ILE 50 at 7, 10, and 15 angstrom in HIV-PRC as opposed to only the first two separations in similar MD simulations of HIV-PRB structures.