A Representation of a Possible Intermediate Step during Substrate Recognition of HIV-1 Protease: Crystal Structures of Substrate Bound Enzyme Exhibiting a Novel Flap Conformation

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HIV-1 protease processes and cleaves the Gag and Pol polyproteins allowing viral maturation and is therefore a prime target of anti-viral therapy. In this study, we are reporting two crystal structures of HIV-1 protease (at 1.85 and 1.5Å), complexed to two variants of nucleocapsid-p1 (NC-p1) substrate, where one of the flaps in each complex is found to be in a relatively open conformation in comparison to the canonical liganded flap-closed conformation. The NC-p1 cleavage site is the slowest and rate determining step in the processing of Gag polyprotein. These structures may represent an intermediate step in substrate recognition in HIV protease and their structures will be compared in detail with similar substrate complexes where the flaps are completely closed that we have previously published.

Keywords: HIV, substrate recognition, enzyme