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Title (English)

Refinement of HIV-1 protease inhibitor crystal structures

Title (Swedish)

Abstract

Structure aided drug design is a technique that can be used to create more efficient enzyme inhibitors by making changes to potential drug candidates in an iterative manner. Using diffraction patterns created by x-ray crystallography, and employing software tools to interpret them, structure models were computed and refined for two instances of HIV-1 protease in complex with the inhibitors Mss329 and Mss332. The final structures showed different patterns of both hydrogen bonds and hydrophobic interactions which could be explained by the CH_2 substitutions in both P1 arms, the removal of a OH group from the P2 arm of Mss332 and the fluorine substitution in the P2 arm of Mss329. The features of both inhibitors could be combined to create a lead compound that would be both effective against point-mutations in the S1 subsite and that would remain effective in smaller doses.

Keywords

HIV-1, Protease, Inhibitors, X-ray crystallography, Refinement, Structures, Fluorine, Molecular Replacement

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