

## ate: a target for HIV therapeutics and vaccines

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HIV-1 infection is initiated by binding of envelope glycoprotein (Env) surface subunit 120 to the primary receptor CD4 and a co-receptor CXCR4 or CCR5, resulting in a series of conformational changes in the Env transmembrane subunit gp41, including insertion of fusion peptide into the target cell membrane and association of C-heptad repeat (CHR) with the N-heptad repeat (NHR)-trimer, a prehairpin fusion intermediate, to form a stable six-helix bundle (6-HB) core, which bring the viral envelope and target cell membrane into close proximity for fusion. Peptides derived from the CHR region, such as T20 (enfuvirtide) and C34, inhibit HIV-1 fusion by binding to the viral gp41 NHR-trimer to block the formation of fusion-active core of gp41. A number of anti-HIV-1 peptides, small molecule compounds, and monoclonal antibodies targeting the gp41 NHR-trimer have been identified, suggesting that the gp41 fusion intermediate is an attractive target for development of HIV therapeutics and vaccines. The presentation will focus on: (1) structure and function of the HIV-1 gp41 NHR-trimer; (2) identification of peptidic and non-peptidic HIV fusion inhibitors targeting gp41 NHR-trimer; and (3) possibility of designing gp41 NHR-trimer-based HIV vaccines.