A Novel Strategy for AIDS Therapy: Anti-HIV Peptides Derived from HIV-1 Gene Products

Dr. Tsutomu Murakami
Chief
AIDS Research Center,
National Institute of Infectious Diseases,
Tokyo, Japan

Abstract
Antiretroviral therapy using a combination of anti-HIV-1 drugs has been successful to treat HIV-1-infected individuals, however, side effects of antiretroviral drugs and the emergence of drug-resistant HIV-1 strains during the therapy has encouraged a search for new types of anti-HIV-1 drugs with different inhibitory mechanisms. We assume that “some of HIV gene products have potential anti-HIV activity”. In fact, Vpr, an accessory protein of HIV-1 was reported to inhibit integrase (IN) activity through its C-terminal domain. We have screened overlapping peptide libraries derived from HIV-1 proteins led to the identification of certain peptide motifs with inhibitory activity against HIV-1 IN. Addition of an octa-arginyl group to the inhibitory peptides caused potent inhibition against HIV replication associated with a significant increase in cell-permeability but also relatively high cytotoxicity. The application of a new class of stabilized \( \alpha \)-helical peptidomimetics to Vpr-derived IN inhibitory peptides led to a remarkable increase in \( \alpha \)-helicity, cell membrane penetration and the expression of potent anti-HIV activity in cells, and also caused a significant reduction of their cytotoxicity. We have also screened overlapping peptide libraries derived from an HIV-1 matrix (MA) protein to find potential anti-HIV-1 activities with novel mechanisms. We found that two MA peptide fragments with or without modification of octa-arginyl group specifically inhibit HIV-1 infection through blocking its entry process, suggesting a role of MA in HIV-1 entry as well as MA as a potential target of HIV-1 infection.

Selected Publications