The CCHC Zinc Fingers of the Retroviral Nucleocapsid Protein Comprises a New Target Useful in Identification and Evaluation of Anti-HIV Therapeutics

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Technology description

Summary

According to a recently released report from the WHO, an estimated 40.3 million people worldwide are currently living with HIV infection, and more than three million people died of AIDS-related illnesses in 2005. In response to increased prevalence of HIV/AIDS, the search for effective antiretroviral therapy is intensive. The present invention describes compounds that may be useful for developing new types of antiretroviral therapeutics for HIV infection.

HIV-1 contains domains known as "CCHC zinc fingers" in the retroviral nucleocapsid (NC) protein. Nucleocapsid CCHC zinc fingers are highly conserved throughout nearly all retroviruses. They are sequences of 14 amino acids with four invariant residues, $Cys(X)_2 Cys(X)_4 His(X)_4 Cys$, which chelate zinc and perform essential functions in viral infectivity. HIV 1 NC has two CCHC zinc fingers, both of which are necessary for infectivity. Many compounds that disrupt the CCHC zinc fingers also inactivate HIV 1 by preventing the initiation of reverse transcription and by blocking production of infectious virus from previously infected cells. Compounds with this activity may be useful for developing new types of antiretroviral drugs. In addition, compounds with this activity can be useful for production of chemically inactivated retroviral particles that lack infectivity but retain structurally and functionally intact envelope glycoproteins. Such inactivated particles may be useful both as in vitro reagents in a variety of applications and as immunogens for whole inactivated virus vaccines.

The present invention concerns antiretroviral compounds that disrupt the CCHC zinc fingers and assays for identifying such compounds. The invariant nature of retroviral zinc fingers also extends the usefulness of these compounds to other retroviruses. Thus these assays are also useful for screening compounds effective against adult T cell leukemia, tropical spastic paraparesis caused by HTLV-I and HTLV-II, feline leukemia virus, feline immunodeficiency virus, equine infectious virus, and lentivirus infections in other animals, and potentially useful for the production of whole inactivated particle vaccines against the pathogens.

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