75

Substance(s) produced by $CD8^+$ T cells from HIV-1-infected individuals can inhibit replication of HIV-1 and HIV-2 via suppression of transcription.

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It has been reported that HIV-2-seropositive women in Senegal had a significantly lower risk of subsequent infection of HIV-1 than did seronegative women, indicating the presence of cross-protective immunity between HIV-1 and HIV-2. $CD8^+$ T cells of HIV-1-infected individuals inhibited *in vitro* replication of HIV-1 as well as HIV-2. The inhibitory effect of the $CD8^+$ T cells on *tat*-mediated LTR transcription of HIV-1 and HIV-2 was in agreement with the inhibitory effect of the $CD8^+$ T cells on *in vitro* HIV-1 and HIV-2 replication. The data suggested that one of the mechanisms in suppression of HIV-2 replication by the $CD8^+$ T cells from the HIV-1-infected individuals might be mediated by downregulation of LTR transcription of HIV-2. Transcriptional inhibition by $CD8^+$ T cells could be mediated largely through a cytokine(s). Molecular as well as biochemical approaches to characterize the cytokine(s) is in progress.

76

Calanolides A and B. Synthesis, Activities, and Structure-Activity Relationships Among Congeners.

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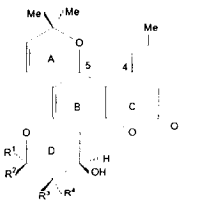

Calanolide A: R^1, R^3 = H; R^2, R^4 = Me
Calanolide B: R^1, R^3 = Me; R^2, R^4 = H

A total synthesis of the nonnucleoside reverse transcriptase inhibitors, calanolides A and B and their stereoisomers, has been achieved (*J. Org. Chem.* **1995**, *60*, 2964), permitting total syntheses of the optically active isomers of congeners of these compounds. Among various ring D isomers, only calanolides A and B show potent anti-HIV activity (EC_{50} ~10^{-7} M, NCI's CEM-SS). Hydrogenation of the A-ring results in retention of activity, while its replacement with various RO- groups at C-5 results in loss of activity, except for cases where the CMe_2 geometry is closely mimicked. A C-5 2-propyloxy derivative rivals the natural calanolides in activity. Alteration of the chain at C-4 by lengthening or addition of polar groups results in diminished activity. Hydroxylation of the double bond in the A-ring results in inactive compounds. (Supported by contract no. N01-CM-47038, DS&CB, NCI, NIH.)