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Combination Studies with Antiviral Compounds to Prevent Reactivation of Latent HIV-1 in OM-10.1 Cells.

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The OM-10.1 cell line is a unique chronically-infected promyelocytic clone which remains CD4+ until HIV-1 activation with tumor necrosis factor-α. A variety of compounds known to have antiviral properties against either acutely or chronically infected cells were evaluated for their ability to inhibit HIV expression in these cells. CD4 cellular expression and the presence of reverse transcriptase were used as markers for quantitating viral expression. Among the forty-eight compounds evaluated, only the nucleoside 3'-fluoro-3'-deoxythymidine (FLT), the cytokine interferon-γ, and the iron chelator desferrioxamine were found to have activity in the OM-10.1 cell system at non-toxic concentrations. The underlying mechanism of action of these compounds is not known. Combination studies will be presented with these antiviral agents with differing structure and mechanism of action in the OM-10.1 cell culture system to determine if synergisitic prevention of viral reactivation is possible.

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Synthesis and Anti-HIV Activity of 2-Substituted, 6-Benzyl-Pyrimidine Derivatives. P. La Colla^, M.E. Marongiu^, A. Pani^, M. Artico°, A. Mai° and S. Massa°. Depts. of ^Biologia Sperimentale, Università di Cagliari, and °Studi Farmaceutici, Università di Roma, Italy.

Acyclouridine derivatives, substituted at both the C-5 and C-6 positions, have been shown to possess potent and selective anti-HIV activity in vitro. Specific target of these compounds is the RNA-dependent DNA polymerase function of the HIV-1 reverse transcriptase. We synthesized and tested for anti-HIV activity a series of 6-benzyl -uracils, -thymines and -5-ethyluracils bearing alkoxy or cycloalkoxy groups in the C-2 position of the pyrimidine ring. Cytotoxicity was assessed by determining the number of viable cells and anti-HIV activity was evaluated by back-titration of the infectious HIV-1 recovered from cell lysates. Several compounds in these series proved to be selective inhibitors of HIV-1 multiplication in vitro. They showed ID50s in the range 100->250 uM and ED90s in the range 1-20 uM. Like HEPT derivatives, none of the test compounds suppressed the HIV multiplication in chronically infected H9/IIIB cells. Spectrum of antiviral activity, target of inhibition and structure-activity relationships will be discussed.

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