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Anti-HIV-1 Activity of Rev and Gag Phosphorothioate Oligo-Deoxynucleotides in Chronically and Acutely Infected Cells.

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28mer phosphorothioate oligonucleotides, sense and antisense whith respect to selected sequences of the HIV-1 rev and gag genes, were synthesized and tested for anti-HIV activity in chronically and acutely infected cells. 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. In both H9/IIIB and MT4 cells, toxicity of antisense oligos (ID50 = 8 uM) was slightly lower than that of the sense counterparts (ID50 = 4 uM). In chronically infected cells, rev antisense was the most potent and selective (ED90 = 0.1 uM , S.I. = 80), followed by the gag antisense (ED90 = 2 uM, S.I. = 4); both the rev and gag sense were inactive at non-toxic doses. In MT4 cells infected at a m.o.i. = 1, rev antisense was again the most potent and selective (ED90 = 0.5; S.I. = 16), followed by the gag antisense (ED90 = 2, S.I. = 4). In this case, however, both the rev and gag sense oligos selectively inhibited the HIV multiplication (ED90s = 1.5 and 0.5, respectively). In MT4 cells infected with a m.o.i. of 0.01, all the oligos showed a selective anti-HIV activity at doses comprised between 0.2 and 0.4 uM. The mode of action of these oligos will be discussed.

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Modulatory Effect of N-Acetyl-Cysteine (NAC) on HIV-1 Multiplication in Chronically and Acutely Infected Lymphocytes.

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In chronically infected monocytes, the TNF-a- and IL-6-induced expression of HIV can be suppressed by NAC and glutathione. Since M/M are believed to be the major reservoir of HIV in the organism, and since plasma and tissue levels of TNF-a and IL-6 increase with the progression of AIDS, the potential therapeutic value of the above thiols has been pointed out. We therefore investigated the effect of NAC on cell proliferation and on the HIV multiplication in chronically and acutely infected lymphocytes. In uninfected B and T lymphocytes and in chronically infected H9/IIIB, NAC exerted a modulatory effect on cell proliferation : doses of 16-1 mM increased, whereas doses of 0.5-0.1 mM reduced the cell growth rate. In H9/IIIB cells, NAC 16-1 mM inhibited the HIV multiplication when the cultures were kept stationary; on the contrary, when the cells were allowed to grow exponentially, NAC stimulated up to ten times the HIV multiplication. In the acute infection, NAC 16-4 mM interfered with virus adsorption (and prevented syncytium formation in cocultures MT4-H9/IIIB), whereas lower doses (2-1 mM) stimulated by 2-3 fold the HIV multiplication. These results indicate that further studies are needed before NAC, or other thiols, are used in the treatment of AIDS.

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