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Differencial Susceptibilities of Two HIV-1 Strains to ddAzThd, ddCyd, ddIno, and PFA in MT-2 Cells. N.K.Ayisi*, S.V.Gupta#, and L.F.Qualtierre+. *Noguchi Memorial Inst., Univ. of Ghana, Legon, Ghana, Depts. of #Vet. Physiology and +Microbiology, Univ. of Saskatchewan, Saskatoon, Canada.

A modified tetrazolium-based colorimetric method was used to test the anti-HIV-1(strains A87SF and A79SK-1) activities of 3'-azido-2',3'-dideoxythymidine (ddAzThd), 2',3'-dideoxycytidine (ddCyd), 2',3'-dideoxyinosine (ddIno), and phosphonoformate (PFA) in MT-2 cell line grown in poly-l-lysine (PPL) coated microtitre plates. Fifity TCID50 of virus per well was used. Percent protection was calculated by the following formula which takes into account, the independent effects of the compounds on the cells:

$$\left[1 + \frac{(OD\text{T})HIV - (OD\text{T})mock}{(OD)mock - (OD)HIV}\right] \times 100$$

where OD=optical density, T=drug treated,HIV=infected, mock=uninfected. The antiviral indices (AI) were determined as the ratios of CD10/ED90. Against strain A87SF, the decreasing order of selectivity (AI) was as follows: ddAzThd (7,037) > PFA (5.8) > ddCyd (3.33) > ddIno (0.5). In contrast, PFA had the highest AI of 20.0, followed by ddIno (6.2), ddAzThd (2.6) and ddCyd (0.7) when tested against strain A79SK-1. The advantages of using (a) PPL coated plates, (b) a fixed amount of virus per well, (c) a modified formula to calculate the percent protection, and (d) ED90 and CD10 to evaluate the selectivity of compounds, will be discussed.

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INTRACELLULAR DELIVERY OF OLIGONUCLEOTIDES WITH ANTIVIRAL PROPERTIES: POLY(L-LYSINE) CONJUGATION AND LIPOSOMES ENCAPSULATION.

Geneviève Degols(1), Patrick Machy(2), Jean-Paul Leonetti(1), Lee Leserman(2) and Bernard Lebleu(1).

(1)Laboratoire de Biochimie des Protéines,UA CNRS 1191, USTL, 34060 Montpellier cedex, France (2)Centre d'Immunologie INSERM-CNRS de Marseille-Luminy, Case 906, 13288 Marseille cedex 9, France

Synthetic oligonucleotides which interact specifically with their complementary nucleic acid sequences, offer attractive possibilities for the artificial regulation of gene expression; applications as antiviral tools are currently under consideration.

Metabolic stability, intracellular target recognition, transmembrane passage and targeting to defined cell tissues still represent major issues within this prospects.

Covalent linkage to poly(L-lysine) improves the efficiency of antisense oligonucleotides directed against vesicular stomatitis virus: antiviral effects were observed at concentrations lower then 1μM. Oligonucleotide delivery from the conjugates is achieved through endocytosis as demonstrated by the use of fluorescent probes and of metabolic inhibitors.

Antisense oligonucleotides encapsulated into antiboby-targeted liposomes resist nucleases and are active against VSV in amounts one to two orders of magnitude less than those reported for unencapsulated oligonucleotides. A double specificity is attained with this delivery system: a cell is selected by the antibody on the liposome and a mRNA is selected in this cell by the complementary oligonucleotide.