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Evaluation of some Novel Compounds for Anti-HIV and Anti-Influenza Activity

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Three novel were first evaluated for cellular toxicity by trypan blue exclusion in peripheral blood mononuclear cells (PBMC's) and continuous cell lines. Anti-HIV assays were performed in PBMC's and a continuous cell line by monitoring p24 antigen in the culture supernatant after pre-exposing uninfected cells to the compounds and subsequent addition of a known titre of HIV. Anti-influenza assays were performed by log reduction of titre of virus for influenza in eggs after direct addition of compounds to virus. Direct HIV inactivation was evaluated by incubation of cell-free virus with the compounds and subsequent titration of the virus in tissue culture. In an attempt to elucidate the mode of action, influenza virus treated in this way was examined by electron microscopy. Electron microscopy revealed that some of the compounds tested appeared to change virus morphology. Compounds were then selected for testing in murine models of HIV and influenza using Rauscher Leukamia Virus and Influenza A respectively. AZT has been used as a control for HIV (or RLV) and amantadine for influenza in all cases. *In vitro*, two of the compounds were active below the toxic level against HIV and Infuenza. *In vivo*, one of the compounds shows antiretroviral activity.

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Screening of anti-retroviral drugs based on inhibition of transformative-destructive effect of mouse sarcoma virus in cell culture.

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We tested more than 70 analogues of nucleosides (AN) for the anti-retroviral activity on the model of Moloney mouse sarcoma virus (M-MSV) infection in mouse cells.The simple and convenient test was based on the ability of M-MSV to induce transformative-destructive effect in mouse cell culture due to propagation of virus. Mouse cells (stable lines C127, NIH 3T3 or primary embryo fibroblasts) were grown in 96-well plates for 18 hours, pretreated with DEAE-dextran, infected with M-MSV and maintained in culture medium, containing different concentrations of tested AN. The results were accounted on 7-th day. As a positive control we used azidothymidine (AZT), that fully suppressed the effect of M-MSV ($10^3 TD_{50}$/well) at concentration 2,5 x 10^{-7}M. The method allowed to estimate not only anti-retroviral activity of tested AN but also their cytotoxicity. The inhibition of transformative-destructive effect of M-MSV correlated with inhibition of virus reproduction. AN under investigation contained modifications in sugar moiety, including acyclonucleosides, nucleosides with substitution at C3' position and those, having modifications at nucleic bases. It was shown that several AN possessed anti-retroviral activity. Combinations of several AN with AZT were tested and in one case a substantial potentiation effect was found.