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Negatively charged albumins exhibit a potent *in vitro* anti-HIV-1 activity and a unique inhibitory action on syncytium formation.

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We derivatized albumin by treatment with sugar derivatives and/or succinic anhydride, yielding negatively charged albumins. They were tested for their anti-HIV-1 activity in MT-4 cells. Succinylated HSA had the most pronounced net negative charge and had an IC_{50} of about 1 μg/ml. No cytotoxicity was observed at concentrations up to 1 mg/ml, implicating a selectivity index (SI = CC_{50}/IC_{50}) of at least 10^3. The sugars per se did not seem to contribute to the antiviral activity. To elucidate the mechanism of action of these anionic albumins we investigated whether they interfered with HIV-1 adsorption to the cells, binding of anti-OKT4A monoclonal antibody (mAb) to the CD4 receptor, binding of anti-gp120 mAb to gp120 or syncytium formation in co-cultures of HIV-1-infected HUT-78 cells with MOLT-4 cells. From these experiments we conclude that albumins with an increased negative charge:
A. cause a 50% reduction of syncytium formation at the same concentration range as their IC_{50} in the antiviral assay.
B. do not bind to the OKT4A epitope of the CD4 receptor and in contrast to dextran sulphate, only partly inhibit anti-gp120 mAb-gp120 interaction and virus-cell binding at concentrations that are a hundred times higher than their IC_{50} in the antiviral assay.
Therefore, we postulate that the modified albumins interfere with the fusion process responsible for virus entry and syncytium formation. An antiviral mechanism that was not reported before.

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A Novel RNA Template for the Study of Antiretroviral Drugs. E. L. White, W. B. Parker, L. J. Ross, S. C. Shaddix, and W. M. Shannon. Southern Research Institute, Birmingham, AL USA.

Reverse transcriptase (RT; EC 2.7.7.49) is a proven target for the development of drugs that are active against retroviruses. Unfortunately, direct comparisons of the *in vitro* activity of different drugs against RT have been clouded by the necessity of using a highly artificial assay system which employs synthetic homopolymers as the templates for the enzyme. In order to better understand the mechanism of action of different drugs, we have developed an assay which uses ribosomal RNA as the template. We believe that a natural RNA template offers a number of advantages for this type of study over the homopolymers that are normally used in the assays of RTs. First, a natural RNA template assay may more accurately represent the true *in vivo* effect of a drug on the activity of RT than assays using a synthetic homopolymer as template and only one deoxynucleotide as substrate. Second, this template, which is commercially available, can be used to study any deoxynucleoside analog regardless of base. For example, the RT from HIV-1 reads only the poly(rA) and poly(rC) templates efficiently making it difficult to study any analog other than those of thymidine and guanosine. Third, comparisons of the potency of different drugs can be made under identical assay conditions. Fourth, synergy or antagonism between deoxynucleoside triphosphates of different bases can be analyzed directly. Finally, this template can easily be adapted to study the incorporation of any deoxynucleotide analog into the DNA by the RT using a RNA template. We have determined the optimal assay conditions for HIV-1 RT with this template and compared them to those for the synthetic homopolymer template poly(rA)•$(dT)_{12-18}$ and for gapped duplex DNA. $MgCl_2$, at 8 mM, gives optimal activity using the RNA template. $MnCl_2$ will not substitute for $MgCl_2$. The K_m for dTTP is 0.57 μM and for the RNA template it is 0.17 μg/ml. The assay has been used to show that AZT triphosphate and carbovir triphosphate are both reversible inhibitors competitive with the expected natural deoxynucleotide substrate with comparable K_i's (0.023 and 0.09 μM). By using the primer extension assay, we have shown that these analogs inhibit the RT by acting as chain terminators rather than by competition with the subtrate. Suramin has an ID_{50} in this assay of 17 μg/ml which is comparable to that reported with a poly(rC)•oligo(dG) template. Most interesting has been the observation that TIBO, a novel non-nucleoside antiviral, has an ID_{50} (0.01 μM) that is lower than the cell culture antiviral 50% endpoint. On the synthetic homopolymer templates, these compounds have ID_{50} values at least 50 times that of their cell culture antiviral activity. Work is in progress to test other types of antiviral compounds with this template and to evaluate the assay with the RT from another human retrovirus, HIV-2.