PA82 Evaluation of gold manno-nanoparticles in a model for DC-SIGN binding and dissemination of HIV-1.

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ABSTRACT TEXT

Background:
One of the major pathways of establishing an HIV infection is the interaction between the virus envelope glycoprotein gp120 and the DC-specific intercellular adhesion molecule-grabbing (DC-SIGN) receptor of dendritic cells. Fourteen gold manno-nanoparticle preparations with variable carbohydrate density were tested in cellbased models to evaluate their effect in inhibiting binding and dissemination of HIV-1 from cells bearing DC-SIGN to T cell populations.

Methodology:
B cells transfected with DC-SIGN were treated with manno-nanoparticles and subsequently exposed to R5 (HIV BaL) or X4 (HIV RF) virus. Effects on binding of the virus to DC-SIGN +ve cells were determined by measurement of p24 antigen. Inhibition of virus transfer from DC-SIGN expressing cells to susceptible T cells was determined by measurement of viral replication, assessed by reverse transcriptase activity. The inhibitory effect of mannonanopartcles on direct infection of $CD4_+$ T cells was also evaluated.

Results:
Manno-nanoparticle demonstrated a wide range of activity (0-90% inhibition) against binding of virus to DCSIGN +ve cells. Compound OM134 inhibited binding of HIV BaL to DC-SIGN by 85%, compound OM92 inhibiting binding by 62%, while free mannan inhibited binding by 60%. Binding of HIV RF was inhibited by 90%, 86% and 79% respectively. Both compounds OM134 and OM92 inhibited trans-infection of T cells by 97%. Surprisingly OM134 also had some activity against direct infection of CD4+ve T cells (PM-1), while the other compounds were inactive.

Conclusions:
We concluded that manno-nanoparticles can directly inhibit HIV-1 binding to $DC\text{-}SIGN_+$ cells and subsequent trans-infection of T cells. Interestingly one compound (OM134) had some inhibitory activity against direct infection of CD4 +ve T cells. The two manno-nanoparticles with the highest inhibitory effect, OM134 and OM92 are similar in size, 1.37nm and 1.5nm respectively. OM134 carries a Man1-2Man residue which has been reported to be critical for binding to gp120. This data suggest that manno-nanoparticles could be utilized in microbicides to block DC-SIGN mediated transmission.

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