48

Dextran Sulfate and Other Sulfated Polysaccharides Induce Persistent HIV-1 Infection.
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Dextran sulfate and other sulfated polysaccharides inhibit HIV infection by preventing the binding of infectious virus to uninfected cells. These compounds are highly active in microtiter antiviral assays and in syncytium-reduction assays. The addition of dextran sulfate to these cultures results in the induction of a low level persistent infection with HIV. These cultures do not exhibit the syncytium formation, high level virus production,and cell killing which is characteristic of productive HIV infection. High molecular weight dextran sulfate (MW 500,000) performs most efficiently in this system while dextran sulfate with molecular weights of 8,000 and 5,000 are less efficient in the induction of persistent infection. The persistently infected culture is characterized by a stable maintenance of the number of infected cells in the culture as measured by syncytium assays and a low level of virus production as determined by quantitation of RT activity and p24 in the supernatant, and ELISA and Western analysis of intracellular HIV proteins. Persistently infected cultures can be maintained for long periods of time without significant change in the number of infected cells. Removal of dextran sulfate results in the initiation of an acute infection with kinetics equivalent to those seen in the absence of dextran sulfate. The addition of dextran sulfate to an ongoing acute infection results in the suppression of the acute infection. In these cultures viable uninfected cells grow while infected cells and existing syncytia proceed to die. Dextran sulfate can be added at a late stage of infection and still effectively rescue uninfected cells from the culture and allow the establishment of a persistent infection. These data suggest that dextran sulfate can be used to establish a cell culture model for a persistent HIV infection. Such a system will be useful in identifying compounds with the ability to kill cells infected with HIV without toxicity against uninfected cells.

49

Anti-HIV Activity of Sulfated Polysaccharides from the Brown Seaweed *Ascophyllum nodosum*. M.M. Klinger and R.W. Buckheit, Jr., Southern Research Institute, 2000 Ninth Avenue South, P.O. Box 55305, Birmingham, AL, USA 35255-5305.

A variety of sulfated polysaccharides (e.g. dextran sulfates, heparin, pentosan polysulfate) are potent and selective inhibitors of HIV-1 in culture. While these polymers inhibit HIV reverse transcriptase in cell homogenates, their anti-HIV activity more likely derives from their ability to interfere with viral adsorption to the cell surface. We report here that sulfated fucans extracted from the brown seaweed *Ascophyllum nodosum* ("rockweed") inhibit HIV infection of cultured CEM cells and block syncytium formation. The two polysaccharide extracts, glucuronoxylofucan (GXF) and ascophyllan (Asco), contain fucose, xylose, glucuronic acid, and sulfate. Gel filtration on Sepharose CL-6B indicates that GXF has an average MW of approximately 30,000 while Asco is a more heterogeneous mixture and is considerably larger in molecular size. The IC_{50} values for the infectivity of CEM cells by HIV-1 are 7.6 and 19.1 ug/ml for GXF and Asco, respectively. The relative effectiveness of the two is reversed in a syncytium-blocking assay using uninfected CEM cells cocultured with HIV-1 chronically infected CEM-RF cells. Both compounds completely block syncytium formation at 100 ug/ml; at 10 ug/ml, Asco blocks 58% of the giant cell formation while GXF has no inhibitory activity. These findings support those of Montefiori et al. (J. Antimicrob. Chemother. 25:313, 1990) that inhibition of HIV-1 cell binding can be distinguished from the inhibition of syncytium formation, suggesting that a mechanism other than gp120-CD4 interaction may be involved in the anti-HIV activity of sulfated polysaccharides. We are currently examining the structural basis for the differential effects exhibited by GXF and Asco. Supported in part by NIH S07 RR05676 (SRI 3888-74).