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Effects of Anti-herpetic Drugs on Ultrastructural Localization of Herpes Simplex Virus (HSV) Glycoprotein D in Cultured Cells Infected with HSV

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We had previously reported that the anti-herpetic drugs (IDU, F3TdR, Ara-A and ACV) had disturbed the envelopment of HSV through reduced production of envelope proteins. In this report, we studied the effects of these drugs on the localization of HSV glycoprotein D which is one of envelope proteins. Monolayers of cells were infected with HSV-1, and were incubated for 12 hours in the presence of the drugs. An indirect enzyme-antibody method was employed for immuno-electron microscopy. In the presence of IDU or F3TdR or Ara-A, the staining of the infected cells were slightly weaker than in the absence of anti-herpetic drug. With ACV, the staining was very much reduced or even absent. These results suggest that mode of inhibition of envelope proteins with ACV is different from that with other anti-herpetic drugs.

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An In Vitro Assay for the Evaluation of Compounds With Potential Activity Against the Hepatitis B Virus.

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A human hepatoblastoma cell line, 2.2.15 (Sells, et al., PNAS 84:1005), which chronically produces infectious Hepatitis B virus (HBV) particles, has been used to develop a practical in vitro assay for the evaluation of compounds with potential activity against HBV. The response of HBV in this culture system to several antiviral compounds (nucleoside analogs) accurately parallels the effects of these drugs on HBV in chronically-infected patients or other hepadnaviruses in experimental animals. For example, a 10 day treatment with ara-AMP (adenine arabinoside monophosphate) had a dose dependent inhibitory effect on HBV replication and extracellular virus production. At the highest dose used, HBV particles were reduced to undetectable levels (>1000-fold depression vs. the day 0 values) and intracellular HBV replication intermediates were reduced over 300-fold. However, as observed in vivo, ara-AMP (which is believed to target the HBV DNA polymerase) (i) did not inhibit HBV RNA or HBV surface antigen production, and (ii) produced only a transient inhibition of HBV DNA production; HBV DNA replication and virion release returned to pretreatment levels within 4 days following the termination of drug addition. Other compounds, such as acyclovir (acycloguanosine) or AZT (3'azido-3'-deoxythymidine), which do not exhibit significant anti-HBV activity in vivo, did not inhibit HBV production in this in vitro assay. Since both intracellular and extracellular HBV DNA forms are analyzed in a quantitative and a qualitative manner in this system, the relative efficacy and mechanisms of action of different compounds which target specific steps in the HBV replication pathway can be evaluated.