102

Duck Hepatitis B Virus DNA Polymerase : Comparison of The Main Properties of Different Enzyme Preparations and The Inhibition by Some Inhibitors, P.Z.Tao, B. Yang, Institute of Medicinal Biotechnology, CAMS, Beijing, P.R.China

Duck hepatitis B virus DNA polymerase (DHBV DNAP) presents both DNAP and reverse transcriptase (RT) activities and plays a key role in DHBV replication. In this study the systemic parallel study of the main properties and the effects of some inhibitors on RT activity in DHBV replicative complexes (RCs) purified from DHBV infected liver and DNAP activity in virions purified from DHBV infected sera was made. Both enzyme activities were dependent on bivalent cations, monovalent cations and nonionic detergent NP-40. The pH optimum of both was pH 8. The concentrition of 50% inhibition (IC_{50}) of PFA, nPredUTP and nPrearaUTP on DHBV RT were 17.0umole, 0.95umole and 7.5umole respectively, while on DHBV DNAP activity were 16.8umole, 0.6umole and 46.4umole respectively. Both enzyme activities were insensitive to PAA. Kinetic study showed PFA was a noncompetitive inhibitor with respect to substrate dTTP with Kii 17.5 umole and Kis 14.5umole and nPredUTP was a competitive inhibitor with respect to substrate dTTP with Kis 0.42umole. Both enzyme activities share the similar properties and sensitivities toward above inhibitors. So either can be used as a target enzyme for the screening of anti-HBV compounds.

103

Characterization of the Anti-human Cytomegalovirus (HCMV) Activity ofThree Anthraquinone Compounds D.L. Barnard, J.H. Huffman, and S.G. Wood Utah State Univ., Logan, Ut, and Murdock Healthcare, Springville, UT

Most anti-human cytomegalovirus (HCMV) compounds which have been developed inhibit HCMV DNA polymerase. Because drug resistant clinical isolates to these anti-HCMV compounds have now been found, a search was begun to find compounds which might inhibit a unique molecular target necessary for HCMV infection. Therefore, a number of anthraquinone derivatives including hypericin, emodin and emodin anthrone were evaluated for anti-HCMV activity biochemical cytotoxicity, and mode of action. Of those compounds evaluated; alizarin, emodin, emodin anthrone, emodin bianthrone, hypericin, quinalizarin, and rhein were active against HCMV. Emodin and alizarin were the least cytotoxic, exerting relatively minimal effects on macromolecular synthesis at doses near the 50% effective doses calculated for the compounds. Since on of the compounds (hypericin) has been shown to be a protein kinase C inhibitor, these seven compounds were also tested for inhibition of HCMV-activated Ca^{2+}, phospholipid-dependent protein kinase activity and purified rat brain protein kinase C. Only emodin showed some inhibition of HCMV-activated Ca^{2+}, phospholipid-dependent protein kinase activity. None of the compounds inhibited purified protein kinase C. These results suggest that these compounds may be used as models for developing a new family of anti-HCMV drugs having a novel molecular target (s).